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THE PATHOGENESIS OF POLIOMYELITIS.[1]

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IN the years between the wars it was common to speak of the tissue tropisms of different animal viruses. The two terms most firmly established were "dermotropic" and "neurotropic", and the only one to survive in common use at the present time has been the term "neurotropic". This has been and is still used to characterize a number of viruses the human importance of which derives from their multiplication in cells of the central nervous system of man. The various viruses causing human encephalitis and poliomyelitis are the most important members of the group of "neurotropic viruses". The investigations of laboratory workers in the 1930's led to an extension of this concept of neurotropic to suggest that these viruses multiplied only in nerve cells. The pathogenesis of diseases caused by these "neurotropic viruses" was therefore thought to be quite different from that of other generalized virus diseases, like the acute exanthemata. Little hope was held out for attempts at immunization by vaccination, for pathologists were obsessed by the idea of the permanent location of these viruses within nerve cells, and their inaccessibility, at any stage of the pathogenesis of the disease, to circulating antibodies.

Since the end of World War II the position has completely changed, and we are all acquainted with the success of the recent large scale American experiments on vaccination against poliomyelitis with the Salk vaccine. Professor Dods has asked me to preface a discussion on the prevention of poliomyelitis by a short account of the modern concept of the pathogenesis of the disease, for the validity of attempts at immunization can be understood only against such a background. To do this I will draw heavily on the investigations of Dr. David Bodian, of Baltimore, who has based his interpretation of the sequence of events in human infection upon experimental infections of chimpanzees and cynomolgus monkeys with poliomyelitis virus. As Bodian points out (Bodian, 1952*a*, *b*), the disease in chimpanzees shows a remarkable similarity to human poliomyelitis. Infection can be established by feeding, subclinical infections with continued excretion of the virus in the fæces are common, and paralysis, lower motor neuron in character, occurs, but is a rare complication. We will therefore examine the pathogenesis of chimpanzee poliomyelitis, and

[1] Based on a lecture delivered to the Australian Pædiatric Association in Canberra on April 23, 1955.

see how investigations at key points in human beings fit in with an hypothesis based on the animal investigations.

Intestinal Phase.

Firstly, the portal of entry of the virus. The concept that poliomyelitis virus enters the body through the exposed ends of the olfactory nerves, popular twenty years ago, is now quite discredited. How then does infection occur? Epidemiological evidence points to the gastro-intestinal tract as the point of entry, and man, chimpanzee and certain monkeys can certainly be easily infected by feeding them with virus-containing foods. There is no certainty about the nature of the cells first invaded, but it appears likely that in both ape and man there are susceptible cells in the tonsillar-pharyngeal region and in the small intestine. Although a few years ago pathologists sought for nerve cell elements in these regions as the site of initial virus multiplication, the experiments of Enders and his collaborators showed that there was no necessity for this, and that the virus might multiply in the ento-dermal cells lining the gastro-intestinal tract. Large amounts of virus are liberated from these cells into the lumen of the gut, and are excreted in the fæces, usually for a considerable period, sometimes as long as four months. It is profitable to think of this stage of polio-myelitis virus infection as the initial or intestinal phase. In the last few years studies in monkeys and man have shown that many infections are limited to this intestinal phase, which is completely asymptomatic. This is almost always the case in individuals in whose blood specific antibody circulates, whether derived from past infection, or from active or passive immunization. Intestinal infections are of no clinical interest, but they are of considerable epidemiological importance for two reasons. Firstly, such infections can result in the production of specific antibody. Secondly, individuals with such infections may disseminate virus widely through the community, perhaps to a greater degree than those with clinically apparent disease, because of their greater mobility.

Viræmic Phase.

If the poliomyelitis virus did no more than cause these asymptomatic infections of the alimentary canal, it would be of no more importance than the majority of Coxsackie virus infections. The human importance of poliomyelitis lies in the occasional occurrence of infection of cells of the central nervous system with the virus. Granted that initial entry occurs via the cells of the alimentary canal, how does the virus pass from these cells to the central nervous system? Impelled by the concept of neurotropism, pathologists for years sought, unsuccessfully, for nervous pathways from the oro-pharynx or small intestine to the central nervous system. In the last few years, however, compelling evidence has been adduced that the virus of poliomyelitis is not confined to nervous pathways. Like the viruses of all other generalized viral infections, there is a blood-stream phase—a stage of viræmia. There is no experimental evidence on the mechanism of entry of virus into the blood, but it is possible that the pathway is similar to that observed experimentally in the pox virus infections of animals (Fenner, 1948). According to this view, multiplication in mucosal cells of the alimentary canal would be followed by release of virus into the lumen of the gut, and consequent excretion in the fæces; and also by movement of virus along the terminal lymph channels to the mesenteric lymph nodes. Positive proof of multi-plication in the lymph nodes is still lacking, although there is some suggestive evidence. If we agree to this temporary hold-up in the regional lymph nodes, what is the next stage? Multiplication of the virus in the lymph nodes and its subsequent release into the afferent lymph vessels, and thus into the blood-stream, will cause viræmia. However, Bodian's (1954*b*) observation that 1000 tissue culture doses of poliomyelitis virus injected intracardially in monkeys disappeared from the blood-stream in five minutes, but caused a severe degree of viræmia a few days later (titres of 10^5 tissue culture doses per millilitre of blood) indicates that the lymph nodes are not the only source of virus. It seems likely that in infections following ingestion the virus entering the blood-stream from the lymph nodes must be taken up by cells lining the vascular system—perhaps the phagocytes of the spleen, liver or bone marrow, perhaps the endothelial cells of the blood vessels themselves. Multiplication in and liberation from these cells would account for the recog-nizable viræmia of the vascular phase of poliomyelitis virus infection. It might be useful at this stage of our dis-cussion to consider the similarity between the mechanisms of infection in poliomyelitis and in mousepox—considering the latter as an example of the group of virus exanthemata. In Figure I, I have tried to indicate the points based on experimental evidence and those which are still speculative, and you will agree that there is still a preponderance of the latter. However, there is every reason to believe that careful experimentation, with the use of existing tech-niques, should allow the picture to be filled in.

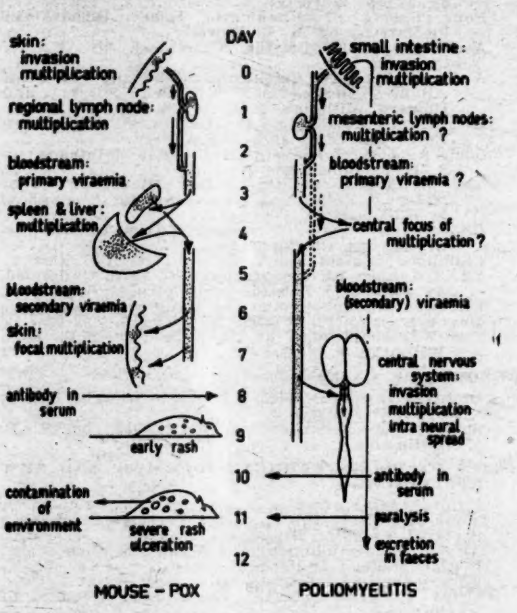

FIGURE I.

Schematic diagram comparing the mode of spread of mousepox virus and poliomyelitis virus in the animal body after infection by natural routes. Experimental proof of certain stages is lacking, and these have been indicated in the diagram by question marks.

Laboratory studies in man and monkey have suggested that poliomyelitis viræmia may occur frequently in the early stages of abortive and non-paralytic poliomyelitis as well as in the paralytic disease (Horstmann, McCollum and Mascola, 1954; Bodian and Paffenbarger, 1954). Indeed, it is possible that the majority of infections in non-immune individuals are associated with viræmia, infections con-fined to the alimentary phase occurring principally in individuals circulating specific antibody.

Viræmia and "Provocation".

It is the stage after the viræmia which poses the greatest problem in poliomyelitis, and constitutes the greatest difference between poliomyelitis and the virus exanthems. In the great majority of cases of smallpox in non-immune individuals, the virus, after circulating in the blood, is localized in the skin and causes the characteristic eruption. In poliomyelitis, however, localization in the cells of the central nervous system is a rare sequel of the viræmia, but is the all-important sequel from the human point of view. Have we any information on the mode of passage of virus from the blood to cells of the central nervous system, or the reasons for such passage in occasional individuals and its absence in the great majority? We must admit at once that we know very little indeed about

the method of entry of virus into the central nervous system, and the factors which may favour or inhibit this. However, there are a few clues. One of these comes from the experimental confirmation in monkeys of McCloskey's finding (McCloskey, 1950) that recent inoculation predisposed to paralytic infection of the involved limb. Bodian (1954*b*) found that monkeys inoculated intracardially with poliomyelitis virus sustained immediate but brief viræmia and substantial viræmia two days later. If they were inoculated intramuscularly or subcutaneously in one limb with gelatin or corticosteroids or penicillin soon after the intracardiac inoculation of virus, there was a profound change in the type and degree of paralysis. Inoculation at the time of viræmia resulted in the very frequent occurrence of paralysis commencing in the inoculated limb —a change in both the frequency and the localization of paralysis occurring after intracardiac injection of the virus in "unprovoked" animals. Bodian believes that the provoking effect of the injections does not act by opening a pathway for passage of the virus upwards along the injured nerve fibres, but rather by altering in a reflex manner the penetrability of blood vessels in the region of the central nervous system which innervates the injected or injured peripheral tissue. This is a problem of critical importance, and it is to be hoped that further evidence of the mechanism of provoking effect will be forthcoming soon. Some such effect may also explain the injurious effects of violent exercise or undue fatigue in individuals who may be incubating poliomyelitis (and who may, therefore, be in the viræmic stage of the disease).

The Neural Phase.

It has been tentatively suggested that the occurrence of the last and vital phase of poliomyelitis virus infection, central nervous system infection, may be dependent upon changes in the vascular penetrability of blood vessels of the central nervous system. Possible reasons for individual variation in the penetrability of blood vessels in the central nervous system, whether determined genetically or by environmental factors, therefore become of major interest, for therein may lie the clue to that infrequent but humanly important complication of poliomyelitis virus infection—paralysis. Twin studies (Herndon and Jennings, 1952) have shown that there is a significant difference between the likelihood of the identical and non-identical twin of an index case to contract paralytic poliomyelitis. Inherited susceptibility was obviously not the decisive factor, for even with the same household environment and the same genetic constitution paralysis involving both members of a pair occurred in only five out of 14 pairs of monozygous twins. Bodian's experiments, just described, suggest the operation of a reflex nervous control of the penetrability of the blood vessels in the central nervous system—effected by stimuli applied peripherally—be they recent injections, violent exercise, recent or old tonsillectomy, or long-standing trauma. And Shwartzman (Shwartzman and Aronson, 1953) has demonstrated that cortisone profoundly modifies the resistance of hamsters and monkeys to intracerebral and intraperitoneal inoculation of poliomyelitis virus.

There is good evidence that within each serological type different strains of poliomyelitis virus vary markedly in their ability to invade the central nervous system (Bodian, 1954*a*). Finally, even if virus invades the central nervous system it does not necessarily cause recognizable symptoms. Bodian and Howe (1945) have demonstrated the frequent occurrence of minor grades of specific damage to nerve cells in monkeys which failed to develop recognizable paralysis. So there is still another variable factor—the degree of neural spread and multiplication after entry of the virus into the central nervous system.

The Immunological Response.

You are all aware that there are three immunological types of poliomyelitis virus, types I, II and III, comparable to the influenza types A, B and C. A difference of major importance, however, is that antigenic variation, so common amongst the influenza viruses, is unknown amongst the poliomyelitis viruses. What is the timing of the antibody response to infection with any of these three immunological types of poliomyelitis virus? As I have indicated in Figure I, detectable neutralizing antibody may appear in the serum within ten to fourteen days of the oral infection of chimpanzees, that is, shortly after the onset of the viræmic phase if this occurs, and antibody titres are usually quite high, in both man and chimpanzee, at the time of onset of signs of central nervous system involvement. It is this latter fact which has been responsible for the failure to appreciate the existence and importance of the viræmic phase, for virus can rarely be recovered in the presence of such levels of circulating antibody. Bodian's (1953) experiments with chimpanzees inoculated with large amounts of antibody to the infecting virus suggested that there were two phases in the antibody response. The first, which occurred only in non-immunized animals, was the rapid rise beginning between the tenth and fourteenth days, which Bodian relates to the viræmic phase of the infection. The second, recognized only in animals which had received enough antibody to prevent the occurrence of the vascular phase, but not to prevent implantation of the virus in the alimentary canal, was a slow rise in the concentration of antibody above the level due to passive immunization, beginning during the fourth week, and resulting in antibody levels at the tenth week comparable to those in non-immunized animals experiencing all phases of the infection. Bodian suggests that this slow rise may be related to antibody production by the regional lymph nodes draining the infected portion of the alimentary canal.

How long does antibody persist at a detectable level? In most communities circulation of all three types of virus ensures reexposure at relatively frequent intervals. In basically immune individuals infection confined to the alimentary tract will often occur, and lead to an increase in the level of circulating antibody. Howe's (1954) report on chimpanzees vaccinated with killed virus showed that antibody titres dropped about tenfold in a two-year period. Infection with the homotypic virus at this stage usually led to an alimentary tract infection and a prompt rise in antibody titre. If the titre of circulating antibody was high at the time of exposure, there was a reduction in the frequency of alimentary infection, in its duration, and in the titre achieved by the virus in its growth in the alimentary tract. The rise in antibody level was greatest when the initial antibody level was low. The situation is exactly analogous to that obtaining in mousepox (Fenner, 1949) and myxomatosis (Fenner, Marshall and Woodroofe, 1953).

Turning to data on human beings, there are only two sources of information. One was the report by Koprowski, Jervis and Norton (1954) that the homotypic antibody level of children fed with living type II virus remained at a relatively high level for at least three years after the virus feeding. In this group reinfection cannot be excluded. Information of a different nature is provided by the studies of Paul, Riordan and Melnick (1951), on the presence of antibody in the sera of Eskimos at Barrow Village in northern Alaska. Figure II, derived from this paper, suggests that in this remote Arctic area type III poliomyelitis virus appeared in 1905, type I in about 1915, and type II in 1930, and that there had been no subsequent exposure to these viruses. The authors are cautious in their interpretation, but suggest that even in the absence of reinfection a considerable proportion of the population exposed to the original infection will continue to circulate antibodies for long periods, perhaps as long as fifty years; a situation reminiscent of yellow fever, in which antibodies have been detected seventy-five years after the last possible exposure to infection (Sawyer, 1931).

Summary.

In summary, we must think of poliomyelitis as a generalized virus infection, in which the virus must follow certain pathways in a well defined sequence as it passes from the fæces of one individual to, in rare instances, the central nervous system cells of another. Firstly, there is the stage of alimentary infection. In the majority of individuals basically immune to the type of virus under

consideration, and in a proportion of non-immunes, infection may be limited to this alimentary phase. It is of importance to the individual in that it acts as a primary immunizing or a booster dose from the immunological point of view; and to the community in that the freely moving individuals with a localized alimentary infection may disseminate the virus widely through the community.

The aim of active immunization against poliomyelitis is to limit all infections to this asymptomatic alimentary phase, or to prevent implantation of the virus in the alimentary tract.

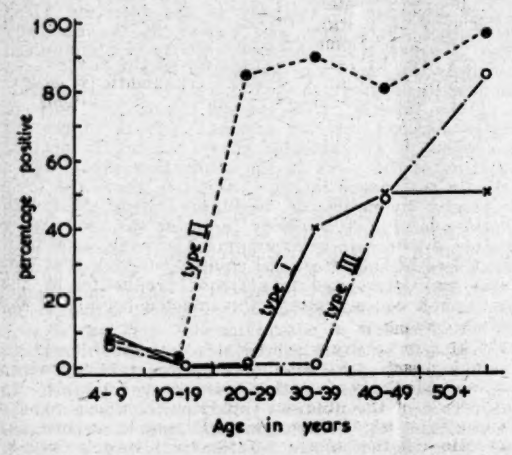

FIGURE II.

The occurrence of neutralizing antibodies to the three types of poliomyelitis virus in Eskimos of Barrow Village in Northern Alaska. [From Paul, Riordan and Melnick (1951).]

In the non-immune individual alimentary infection may be followed by passage of virus through the regional lymph nodes into the blood-stream, and secondary localization and multiplication in cells associated with the vascular system. Recognizable viræmia ensues and this may constitute the extent of the infection. Such infections cause the symptoms associated with the diagnosis of abortive or non-paralytic poliomyelitis.

In some non-immune individuals the virus may enter the central nervous system directly from the blood-stream, and undergo secondary spread along neural pathways within the central nervous system. Depending on the degree and severity of this neural phase, the disease may vary from very mild to severe paralytic poliomyelitis. Genetic background, hormonal factors, and reflex changes in the penetrability of the blood vessels of the central nervous system may all play a part in determining the occurrence and extent of central nervous system invasion. Finally certain strains of virus are much more invasive than others (Bodian, 1954*a*), and such strains, introduced into populations with a low immunity to that serological type of virus, may produce epidemics characterized by severe paralysis.

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INTRODUCTION TO A SYMPOSIUM ON RHEUMATIC FEVER.[1]

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IN our vaunted control of the infectious diseases — an achievement of which we are justly proud — it is sometimes forgotten that there are three important exceptions, namely, influenza, poliomyelitis and rheumatic fever. Largely because these are unsolved problems, they attract many of the best minds of our generation. I would say that influenza and poliomyelitis are easier problems than rheumatic fever, because in influenza and poliomyelitis we have experimental animals, we have many reliable tools of investigation, the ætiology is certain, and the pathogenesis is now fairly well understood. All that remains in the control of these two diseases is to discover a practical way of raising and maintaining the community's resistance by immunization. Indeed, in poliomyelitis we are well on the way to attaining that objective, thanks to the work of Enders and his colleagues in finding a method of obtaining a supply of the virus in tissue culture.

But in rheumatic fever[2] there is no experimental animal, reliable tools of investigation are still to seek, and although there are some clues in the ætiology, pathogenesis

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

[2] It might be questioned whether rheumatic fever is an infectious disease in the strict sense of the term. However, it is now generally accepted that rheumatic fever has an infectious basis.

and control of the disease, they are still seen through a glass darkly. No one would lightly undertake to discuss rheumatic fever in the present state of our knowledge.

Incidence.

Before I take up the ætiology and pathogenesis of rheumatic fever, I should like to say something about its incidence. In a disease so serious both in its acute stages and in its sequelæ, we should have some idea of the extent of the problem. I do not think it is enough to say that rheumatic fever is now the most serious of all diseases in the five-to-fifteen age period, and the cause of much long-standing disability.

The problem of incidence can be approached from three angles—mortality, morbidity and post-mortem figures.

Mortality.—Some years ago Glover reported that deaths from rheumatic fever in England had fallen from 60 per million in 1915 to 20 per million in 1940. Glover correlated this fall with the declining mortality from scarlet fever, which is a world-wide phenomenon. Dr. H. O. Lancaster informs me that the mortality from rheumatic fever in Australia was 51 per million in 1915 and 32 per million in 1940. These mortality figures do not throw much light on the real incidence of rheumatic fever, in that they reflect only the mortality in the acute stages of the disease. However, they do suggest that the incidence is declining.

Morbidity.—Notification figures are the obvious source, but are unreliable for two reasons — firstly that doctors often forget to notify, and secondly that notification figures do not take into account the milder forms of the disease, and it is certain that many children do not present the classical and easily recognizable picture of rheumatic fever. For these reasons morbidity has been investigated by conducting clinical surveys of school children in the hope that such surveys would give a more accurate figure of the true incidence. Without going into detail, these surveys, both in Australia and in America, agree fairly well that 0·5% to 0·8% of school children show clinical evidence of having been affected with rheumatic fever. Admittedly the criteria on which these clinical surveys are based are somewhat controversial.

Post-Mortem Evidence.—There is considerable variation in what figures are available. The Royal Prince Alfred Hospital in Sydney reported an incidence of 1·2%; the Royal Adelaide Hospital reported an incidence of 3·8%; and the Peter Bent Brigham Hospital in Boston reported 4·5%.

From all these figures it is difficult to draw any firm conclusion as to the incidence of rheumatic fever. I would suggest that at least 1% of the population suffer from the disease at some time during their lives.

Ætiology and Pathogenesis.

Robert Hutchinson once remarked that in any disease of unknown ætiology there were three guesses—virus, deficiency, allergy. Hutchinson was speaking of pink disease when he made the remark, but it is true of rheumatic fever also. Some years ago English workers made claims for a virus ætiology, but the work was not confirmed and a virus ætiology does not fit the picture of rheumatic fever. Then a lack of vitamin *C* in the diet was put forward and then given up. It is true that the disease appears more commonly in low-income families, but before we invoke nutritional deficiency we must remember that crowding is more common in such families, and crowding means a greater incidence of upper respiratory pathogens.

The most widely held ætiological theory today is that rheumatic fever is an allergic phenomenon linked in some way with an infection by *Streptococcus pyogenes* (hæmolytic streptococcus Group A). In the 1920's that old pseudovillain the green streptococcus was the popular fancy, but in the 1930's Coburn put forward much more convincing evidence for *Streptococcus pyogenes*. This author pointed out that the usual sequence of events was a streptococcal tonsillitis from which the patient recovered, a latent period of two, three or four weeks, and then rheumatic fever. Further, he claimed that if the patient recovered from this primary attack of rheumatic fever, a relapse was likely after another streptococcal infection. I think it is generally agreed today that *Streptococcus pyogenes* is the first link in the chain of events which lead to rheumatic fever, but we are still groping in the dark about the other links in that chain.

There is much to be said for the allergic hypothesis, the comparative rarity of rheumatic fever following on streptococcal infections, which are so common, the greater susceptibility rather than immunity to subsequent attacks of rheumatic fever, and the tendency of rheumatic fever to run in families, suggesting a genetic susceptibility. All the above facts are consistent with what we know about the characteristics of allergic disease. But if rheumatic fever is an allergic phenomenon, there must presumably be an antigen and an antibody as the basis of the allergy. We know nothing of this hypothetical rheumatic fever antigen and antibody, although we suspect that the antigen and antibody must be linked in some way with *Streptococcus pyogenes*. The expression "linked with the streptococcus" is used, because there is no good evidence that the rheumatic fever antibody is directed to the streptococcus alone or to any of its products. A plausible hypothesis is that a tissue protein is altered by the streptococcal infection, and that this altered tissue protein is antigenic. However, this is pure hypothesis.

It is known that there are two distinct kinds of allergy, which differ in their mechanism, and we should attempt to find out to which kind of allergy rheumatic fever belongs. In the first kind of allergy, of which pollen allergy is typical, the skin reaction to the antigen is immediate, the reaction is mediated by histamine, and the antibody is free in the serum of the allergic subject. In the second kind of allergy, of which tuberculin allergy is typical, the skin reaction to the antigen is delayed (twenty-four hours), the reaction is not mediated by histamine, and the antibody is not free in the serum of the tuberculin-sensitive subject. The only clue we have about rheumatic fever is that its symptoms respond to cortisone, resembling tuberculin allergy, which is influenced by cortisone, while pollen allergy is not affected by the hormone. If on this analogy the allergic mechanism of rheumatic fever resembles the mechanism of tuberculin allergy, we would not expect to find the rheumatic fever allergic antibody free in the serum. Laboratory workers for many years have been searching the serum of rheumatic fever patients for a diagnostic antibody, using different fractions or products of *Streptococcus pyogenes* as the antigen. What has been found is, on the average, a higher titre of antibodies in rheumatic fever patients; but, though this is helpful, no definite conclusion can be drawn from the titre of the antibody in any particular case. Unfortunately we have no method of detecting the rheumatic fever antibody on the cells of the rheumatic fever patient, although in my opinion that is where the antibody is more likely to be present.

Natural History of Rheumatic Fever.

Curiously, the disease is comparatively uncommon in very early childhood. While the greatest incidence is in the five-to-fifteen age period, the disease is not restricted to childhood, as witness the high attack rate in recruit camps following epidemics of streptococcal tonsillitis.

American observers estimate that approximately 3% of patients suffering from streptococcal tonsillitis subsequently develop a primary attack of rheumatic fever, and that some 50% of subsequent attacks of tonsillitis precipitate a recurrence of rheumatic fever. These figures of 3% and 50% are only approximations, but they emphasize the much greater danger of tonsillitis once the primary attack has occurred. Naturally, one asks the question: "Why only 3%?" Nobody knows.

Turning to the subsequent development of the disease, it was estimated before the days of penicillin that half the patients who recovered from the primary attack of rheumatic fever without apparent cardiac damage subsequently showed evidence of rheumatic heart disease. This damage to the heart could occur without obvious

recurrent attacks of streptococcal tonsillitis or overt recurrences of rheumatic fever. It would appear that if acute rheumatic fever becomes quiescent and is not lighted up by subsequent attacks of tonsillitis, the patient may recover completely or the disease may enter a chronic phase which results in cardiac damage. Supporting evidence for this chronic phase is the finding of Aschoff bodies in a high percentage of atrial tissues removed in operations for mitral stenosis. Can penicillin prevent this chronic phase? It is yet too early to say.

There is one aspect of the natural history of rheumatic fever which has received scant attention. We know it is a long disease if the patient does not recover completely after the primary attack. Where is the streptococcus through the long years, if indeed it is present at all? If it is not present, how are we to explain the Aschoff bodies at the operations for mitral stenosis? We know that in the acute phase of the disease it is often difficult to find the organism in the throat, and it is certainly not in the blood stream. Yet some workers in England were able to demonstrate the presence of *Streptococcus pyogenes* in the internal organs and in the heart lesions in careful post-mortem examinations of patients dying in the acute stage. It is to be hoped that pathologists will give some attention to the bacteriology of the tissues when the opportunity occurs. Even a negative finding would be more valuable than no information at all.

Treatment.

Clearly the detail of the management of the rheumatic fever patient is outside my competence. I suppose it was the disappointing results with the sulphonamides which at first inhibited the treatment of the active disease with penicillin. The importance of eliminating the streptococcus has overcome this inhibition, and I would advocate an adequate course of penicillin. The all-important question is whether subsequent cardiac damage can be prevented by adequate doses of penicillin in the active phase. I would think that the outlook is encouraging but not certain.

Prophylaxis.

This part of the subject is better considered under two headings — prophylaxis against the primary attack and prophylaxis against subsequent attacks.

Prophylaxis against the Primary Attack.—While it is true that rheumatic fever is a comparatively rare sequela of streptococcal tonsillitis, we have no way of telling which patient will subsequently develop rheumatic fever. Hence the only practicable prophylaxis against the primary attack is to eliminate the possibility by treating all patients suffering from streptococcal tonsillitis with adequate doses of penicillin. There is now good evidence that penicillin treatment of tonsillitis will prevent the subsequent development of rheumatic fever, but that sulphonamides are useless as a prophylactic against the primary attack. This failure of the sulphonamides is most unfortunate because these drugs are much easier to administer than penicillin and will doubtless continue to be prescribed in the treatment of tonsillitis.

One is tempted to raise the question of the bacteriological diagnosis of streptococcal tonsillitis, and while that is desirable, let us be serious and recognize that for one reason or another, or both, in the great majority of instances the swab will not be taken and cultured. The diagnosis will then be clinical, and if it is helped by a scarlet rash, so much the better. One must not forget, too, that the patient with a mild streptococcal throat will probably not be taken to the doctor, and one can see no way of meeting that difficulty.

Prophylaxis against Subsequent Attacks of Rheumatic Fever.—Recent reviews of sulphonamide prophylaxis, which was introduced some fifteen years ago, indicate that this form of prophylaxis reduces recurrences by about 85%. How, then, are we to explain this apparent paradox—that sulphonamide treatment of tonsillitis does not prevent the primary attack of rheumatic fever, yet sulphonamide prophylaxis does prevent recurrence fairly successfully? One must remember that the sulphonamide drugs are essentially bacteriostatic and moreover are inhibited by the presence of pus. It would appear that in treating the established streptococcal lesion in the throat with sulphonamides one is asking too much of the drugs, whereas in prophylaxis against streptococcal infection they are given a task more suited to their capacity as bacteriostatic agents. Modern opinion is veering towards penicillin prophylaxis against recurrent attacks of tonsillitis, and evidence is accumulating that it is effective. If the aim is to eradicate the streptococcus rather than to suppress the organism, which seems a reasonable and desirable objective, then penicillin has better claims than the sulphonamides. Moreover, a penicillin-resistant *Streptococcus pyogenes* is unknown, whereas sulphonamide-resistant streptococci have been reported.

To sum up, we have in penicillin a promising weapon in the treatment and control of rheumatic fever. The future will disclose how good it is and what are its limitations. A well-conducted clinical trial in such a long-drawn-out disease is not an easy task, but is an essential part of the rheumatic fever problem.

FOUR FACETS OF RHEUMATIC HEART DISEASE IN PÆDIATRICS.[1]

By M. L. POWELL,
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THAT curious tuberculin-like, allergic phenomenon called the rheumatic process extends to many tissues of the body. Apart from the rare maniacal chorea, the only region affected which causes real worry is the heart and its coverings. In fact, it has been an impression that the more definitely other regions, such as joints, are affected, the less affected is the heart.

Certain it is that some of our patients with the worst hearts have a past history utterly without suggestion of rheumatism.

CLINICAL CLASSIFICATION.

It is possible, I think, to subdivide the clinical happenings in the cardiac field into four main groups. Though perhaps artificial and with manifest overlap, I have found it helpful as a teaching and prognostic method.

Group I.

Group I is the all-important group. It represents the initial process of cardiac involvement during an attack of rheumatism, the general manifestations of which can be clear cut and "classical" with preceding sore throat, joint pains, sweats, pallor, fever, *et cetera*, or more commonly can be dangerously insidious, with merely pallor, abdominal pains, slight fever and anorexia—that is, the patient is simply a vaguely ill child.

All too often we have watched this sinister process swing, like the predicted hurricane, towards the region which really matters—the cardiac environs—and we have all watched the ruthless destruction of those vital structures, the cardiac valves.

It is in those few weeks that we must exploit to the full such treatment as we have.

The Cardiac Manifestations.

Of the three structures, valves and myocardium and pericardium, the valves appear to me to be most important. These tiny structures (the mitral valve is one-sixtieth of the cardiac mass; the aortic valves much less) are in hæmodynamic control of the intracardiac circulation. The valves must always "seat" well. Severe degree of destruction can, of course, be disastrous, but minor degrees of damage, distortion, and consequently bad "seating", whilst

[1] Part of a symposium on rheumatic fever, held at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

not immediately troublesome, will inevitably place strain on cardiac efficiency.

Severe grades of myocarditis, with extensive Aschoff body formation with its muscle disintegrating effect, can, of course, also be rapidly fatal, particularly if, as usually happens, the valves are simultaneously destroyed. But I believe it is possible to have severe myocarditis, minimal or no valve damage, bruits being produced by a functional regurgitation from cardiac dilatation, and complete recovery. Similarly, pericarditis has not the significance of valvular damage.

The signs of cardiac involvement are usually definite. The cardiac action is increased in force and usually in rate, but one must not be deceived by a relatively slow rate of, say, 98 per minute with a temperature of 102° F., for this occasionally occurs. The force of the cardiac thrust is in contrast to the quiet heart of the virus myocarditis.

A systolic murmur is invariably present in the mitral area at some stage, and it is due to imperfect "seating" of the valve cusp which allows regurgitation. This failure of the valve to "seat" is due either to dilatation of the mitral ring or to distortion or vegetation formation on the valve. I doubt if it is possible with certainty to establish which is the cause in any given case, but it is my impression that the harsher the murmur, the more likely is it to be valvular involvement and therefore more likely to be permanent, and the case to graduate into Group II. On the other hand, the soft mitral systolic bruit in the slightly dilated heart can be reversible.

A more striking and at times more ominous finding at the apex is the addition of a mid-diastolic bruit which produces a triple rhythm. This is due to the receipt by the left auricle of a gross overfilling with each ventricular systole, and an emptying back during ventricular diastole. Left auricular systole, which one would imagine should produce a presystolic bruit, is ineffective as the ventricle is already partly filled—a state of affairs not obtaining in mitral stenosis.

These children are obviously ill; they are the ones who can rapidly die, and paradoxically they can make complete recovery, provided, and this must be stressed, they are lucky enough to have myocarditis only with minimal valve damage.

It is in this type of case, and they stand out because the patients are so severely ill, that I have seen, I think, the steroid hormones at their therapeutic best. I find myself ignorant, however, on the point whether, in later life and in the absence of further attacks, the myocardium may give evidence of its childhood's pathological change.

This, then, is Group I, the primary complex of rheumatic carditis. It demands early diagnosis. It may on occasions spontaneously recover without overt damage to the heart. If Illingworth is right, and we owe him a debt for a brilliant clinical and statistical survey, this is the group which will require as basic management rest, cortisone, high dosage with salicylates, and penicillin. It will also demand the best possible prophylactics against recurrence, and I am interested in the extraordinarily favourable reports on orally administered penicillin in this regard.

Group II.

Group II is the natural outcome of Group I. The fact that a patient in Group I will enter Group II can be predicted in many cases during the course of the initial illness. We see the patients as follow-up cases. Many are outwardly well, but they have their hallmark of rheumatism in the form of a mitral systolic bruit, which is sometimes picked up in routine examination in a well child, and sometimes by discovery of a rather full left upper cardiac border indicating that the left auricle is a little dilated. The pulmonary second sound is loud and split. Other patients show no signs of cardiac embarrassment at all, and play all games. They may lead quite an active life with minimal disability, but a proportion proceed later to mitral stenosis. If they are unfortunate enough to have an aortic lesion as well, the prognosis is more grave, as the left ventricle has now two serious impediments to its output. The general purpose here is to prevent recurrence. My information is that orally administered penicillin is far superior to sulphonamide in this respect.

Group III.

Group III includes the wrecked hopeless heart of rheumatism. All are familiar with these unfortunate children. The children may have had one, but usually more, attacks and with each there has been progressive destruction and distortion of valve tissue. The heart is huge; the children never have a chance to reach the stage of mitral stenosis, for when one examines the mitral valve at the inevitable post-mortem examination, there is often a gaping orifice capable of taking two fingers. The only intact valve is the pulmonary. No hæmodynamic control is possible within the heart, and variable murmurs are present all over the precordium. The patients are admitted to hospital in recurrent bouts of cardiac failure, and sometimes make astonishing temporary recovery; but the myocardium battling valiantly against impossible hæmodynamic odds finally fails. The only treatment is that for the cardiac failure.

Group IV: Mitral Stenosis.

I mention the mitral stenosis group only to indicate that our pædiatric age limit of fourteen years gives inadequate time for stenosis to appear. The true presystolic murmur and slapping first sound are an extreme rarity, but recently we had two definite cases; in one catheterization revealed the characteristic high pulmonary capillary pressure.

Rheumatic carditis can occur at an early age—Dr. Alan Williams performed a post-mortem examination on a boy of two and a half years recently with gross mitral valve damage. Had that boy's lesion been less severe, mitral stenosis could conceivably have occurred before fourteen years of age.

ACCIDENTAL POISONING IN CHILDHOOD.[1]

By F. W. CLEMENTS,
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The Extent of the Problem.

ACCIDENTAL poisonings occupy a relatively minor place among all the causes of accidents which are suffered by children and are responsible for deaths. Two sources of data are available from which estimates can be made of the extent of this problem. One is the results of a survey of children for accidents, and the other is the official "Demography Bulletins", which give mortality figures.

In 1952 a survey was made of some 23,784 children (12,131 boys and 11,653 girls) under the age of eight years to ascertain the accidents sustained by them from birth to six years of age. The general accident pattern and the details for traffic accidents and for burns and scalds sustained by these children have already been published (Clements, 1955*a*, 1955*b*, 1955*c*), and further reports on other types of accidents will appear later. Table I shows the numbers and percentages of accidental poisonings at each year of age.

From this table it will be appreciated that accidental poisonings constitute relatively small percentages of the accidents from which pre-school children suffer; at no age do they exceed 9% of the total number of accidents recorded for the children studied. This low figure is partly due to the large number of falls which dominate the accident picture of childhood.

Table II, which is constructed from data in the "Demography Bulletins", shows that a higher percentage of accidental deaths is due to poisoning compared with

[1] Read at a round table conference on accidental poisoning in childhood at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

TABLE I.

Accidental Poisonings at Each Year of Age.

Age Groups.	Males.				Females.			
		Accidental Poisonings.				Accidental Poisonings.		
	Number Exposed.	Number of Children.	Rates per 1000 Children.	Percentage of Total Accidents Due to Poisoning.	Number Exposed.	Number of Children.	Rates per 1000 Children.	Percentage of Total Accidents Due to Poisoning.
Under one	12,131	8	0·66	3·3	11,653	7	0·60	3·9
One year	11,727	37	3·07	5·6	11,481	43	3·75	8·1
Two years	10,690	111	10·38	8·8	10,583	54	5·10	5·7
Three years	10,690	54	4·86	4·0	10,583	25	2·36	1·7
Four years	10,690	22	2·06	1·9	10,583	7	0·66	0·9
Five years	10,690	3	0·28	0·4	10,583	6	0·57	1·1

the percentage of non-fatal accidents due to accidental poisoning. This difference is explained by the relatively large number of minor non-fatal accidents reported in the survey.

TABLE II.

Mortality Due to Accidental Poisonings, 1950 to 1952.

Ages in Years.	Death Rates per Million.		Percentage of Total Accidental Deaths Due to Poisoning.	
	Male.	Female.	Male.	Female.
Less than one ..	6·8	3·6	4·7	3·2
One	106·2	59·3	19·4	15·5
Two	14·3	41·2	3·7	19·3
Thre	14·2	14·8	4·8	9·3
Foure	7·0	7·7	2·9	6·3

It is worth recording at this stage that the death rates for accidental poisoning in childhood in Australia are increasing. Also, the death rates are significantly higher than in the United States of America and the United Kingdom. The combined death rate for males and females one to four years of age for accidental poisoning for the years 1950-1952 for Australia was 3·3 per 100,000, compared with 2·6 per 100,000 in the United States of America and 1·2 per 100,000 for the United Kingdom.

The Nature of the Problem.

Incidence by Age and Sex.

From Table I it will be seen that up to two years of age the incidence rates for boys and girls are similar. After this age the rate for boys is significantly higher than that for girls. The peak for both sexes occurs at two years of age. By contrast the death rates are much higher for children one year of age. If the two sets of data are combined, this difference suggests a higher case mortality rate at one year of age. This poses two questions: Are the younger children more susceptible to the effects of poisons? Is there a longer delay with younger children in seeking first aid because at this age the children are less vocal?

Position in Family.

The position in the family of the 372 children who swallowed a poison was studied against the distribution of the total number of children investigated in the survey. The analyses showed an absence of pattern. Position in the family did not appear to have any influence on whether or not a child swallowed a poison.

Types of Poisons Swallowed.

The survey data showed that some sixty poisons were swallowed by 374 children. Similar surveys both in this country and abroad have produced the same long lists of household, garden and farm commodities and pharmaceutical drugs. Nothing is to be gained by quoting a list of the items swallowed. They have, however, been grouped into nine categories, which are shown in Table III with the numbers of children involved.

As in other Australian surveys, kerosene dominates the list, followed closely by pharmaceutical preparations and other chemicals.

Accessibility of Poisons.

The results shown in Table III suggest that the majority of poisons were left within easy access of the children.

TABLE III.

Accessibility of Poisons.

Nature of Poison.	Degree of Accessibility.								Total.	
	Within Easy Access.		Child Climbed to Obtain.		Taken from a Cupboard at Ground Level.		Given by Another Child.			
	Male.	Female.	Male.	Female.	Male.	Female.	Male.	Female.	Male.	Female.
Liquid pharmaceutical preparation ..	9	3	1	—	3	2	1	—	14	5
Tablet or pill pharmaceutical preparation	23	11	12	7	5	7	—	—	40	25
Kerosene	57	36	6	—	5	—	2	1	71	37
Caustic soda	6	4	—	—	—	—	—	—	6	4
Other chemicals	46	30	11	4	4	2	1	—	62	36
Turpentine	9	4	1	—	2	—	—	—	12	4
Ant poison	9	7	2	1	—	—	—	—	11	8
Fly spray	6	6	—	—	2	—	—	—	8	6
Paint	1	1	2	1	—	—	1	—	4	2
Total	166	102	35	13	21	11	5	1	227	127
Percentage	73	81	16	10	9	9	2	—	100	100

TABLE IV.
Severity of Effect of Poison Swallowed on Child.

Age in Years.	Males.			Females.		
	Total Number Who Swallowed Poison	Seriously Ill.		Total Number Who Swallowed Poison.	Seriously Ill.	
		Number.	Percentage.		Number.	Percentage.
Under one ..	8	2	—	7	1	—
One	37	11	30	43	10	23
Two	111	25	21	54	9	17
Three	54	4	7	25	7	28
Four	22	3	—	7	2	—
Five	3	—	—	6	1	—

and that, contrary to popular belief, most children who accidentally swallow poisons do not have to climb to difficult places or open securely fastened cupboards.

Severity of Effect of Poison Swallowed.

The criterion for judging severity was the method of treatment followed. If the child was admitted to hospital, he was placed in the severely affected group. It is recognized that it is the practice of most hospitals to admit children who have reputedly swallowed some types of poison irrespective of the presence of symptoms. Many of these children do not develop symptoms after admission to hospital.

Table IV shows that the highest incidence of severely affected boys was in the one-year-old group, the incidence decreasing for the next two age groups. For girls the pattern is different, with the highest incidence of severely affected in the three-year-old group. The numbers in this age group are small, but it would require a considerable shift from the severe to the mild group to bring the percentage of severely affected girls at this age to the same percentage as the boys. There was no information in this survey to suggest reasons for this difference.

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A SOCIAL STUDY OF ACCIDENTAL POISONING.[1]

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AND

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ACCIDENTAL POISONING occurs commonly in young children. In Australia, Clements (1955) in a recent survey estimated that approximately one child in 350 under the age of six years swallowed a poisonous substance. During the years 1950 to 1952, 76 children under fifteen years of age died of poisoning, that is, approximately 25 per year (Commonwealth Bureau of Census and Statistics, "Demography Review", 1950, 1951, 1952). In the United States of America over 400 deaths occur each year (Bain, 1954), and Wheatley (1953) estimates that for every death there are at least 100 serious cases. In Britain 218 children died from poisoning in the decade 1940 to 1949 (Swinscow, 1953). Relatively few social studies have been conducted on poisoning, and such studies have been largely of the selected group of children admitted to hospital.

[1] Read at a round table conference on accidental poisoning in childhood at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

The basis for prevention must come from knowledge gained by adequately investigating a representative sample of the homes of all children who accidentally take a poisonous substance. This study was undertaken in Melbourne in an attempt to answer the following questions: How common is this accident? From what social classes do these children come? Is there a particular type of home from which many of these children come? What is the standard of parental care exercised by these parents? Is a particular type of child likely to take poison? How commonly is poisoning due to negligence, how often is it an unpreventible accident, and how often is it preventible? If these questions can be answered, then a sounder basis for prevention will be established.

Material and Method of Study.

During a period of forty-eight weeks (April, 1954, to March, 1955) 419 children attended the Royal Children's Hospital for treatment of accidental poisoning. Details of all patients were recorded. The circumstances of the accident, and social background and homes of 155 patients were investigated in detail by an experienced medical social worker. The 155 homes studied were composed of a sample of 70 of 97 patients admitted to hospital for treatment and of 85 of 322 patients treated as out-patients and allowed to go home the same day. Information obtained by interviewing the mother and observing the home was recorded under the following headings:

1. *The Home.* Homes were divided into three types, good standard home, fair and poor. The criteria for a good standard home were that the building was in good repair, was clean throughout and had an adequate kitchen, separate bathroom and laundry facilities with running water, suitable lighting and satisfactory toilet arrangements. Sleeping accommodation was such that no more than two persons occupied each room. The fair and poor homes were classified according to what proportion of the above essentials was missing.

2. *Social Class of the Family.* The social class of the family was graded according to the classification used by the Registrar-General of England and Wales as summarized in the Medical Research Council of Great Britain (Special Report Series, 248, 1944). In this classification social classes are graded into five groups according to occupations: (*a*) professional persons and business executives, (*b*) employers and managers of wholesale and retail businesses, (*c*) skilled tradesmen, (*d*) semi-skilled workers, (*e*) labourers.

3. *The Mother.* An assessment was made of the mother's intelligence, the standard of housekeeping, the quality of care and supervision which she gave her children, and of her emotional attitude to them. Three grades of very good, average and below-average were established.

4. *The Type of Child.* A record was made of the child's development and characteristics and any behaviour deviations. The circumstances of any previous poisonings and accidents were noted.

5. *The Circumstances of the Poisoning.* The circumstances of the poisoning included details of how the child obtained the substance and of its accessibility at the time

of the accident and also at other times. Note was made of the parents' awareness that it was a poison and the precautions which they took with other poisonous substances.

Age Incidence.

The age incidence is set out in Table I.

TABLE I.

Age in Years.	Number of Cases.
0 to 1	18
1 to 2	189
2 to 3	125
3 to 4	52
4 to 5	16
5 to 6	6
6 to 15	13
Total ..	419

Sex Incidence.

There were 232 boys and 187 girls who took poison.

Age and sex grouping follows the typical pattern of most reported series.

Deaths.

Only one death occurred, that of a boy of two years and seven months, who swallowed colchicum and salicylate tablets.

Types of Poisons.

One hundred and fifty-two different types of poison were taken by the 419 children. This wide variety of substances is most conveniently grouped as follows:

Medicaments. The medicaments totalled 193; 147 were internal and 46 were external. Ninety-two children took the following drugs: phenobarbital, aconite, aspirin, "Laxettes", "sulpha" tablets, iron and ergot preparations, and "Dexedrine". Pills or tablets were the common preparations taken; fluids were taken sometimes, but rarely pastes or ointments.

Substances in Common Household Use. Substances in common household use totalled 174; of these, 97 were petroleum products, and others numbered 77. Eighty-five children swallowed kerosene. Forty-four children took turpentine, or preparations containing caustic soda or one particular brand of furniture polish.

Miscellaneous. The miscellaneous group totalled 52. Forty children took pest control poisons, garden sprays or paints.

Type of Home and Social Class.

Of the 155 homes visited, 63% were good standard homes by reason of the size and repair of the home, the general facilities and the standard of housekeeping; 21% were fair standard homes, while 16% were substandard because of structure or household neglect or both.

In classification of the families by the fathers' occupations, 28·5% were in social classes 1 and 2, 50·5% in social class 3, and 21% in classes 4 and 5. The type of home and social class corresponded closely. The greater number of children lived in good standard homes and came from the economically secure groups of professional and business classes and skilled tradesmen.

Standard of Maternal Care.

The standard of maternal care was assessed in 26% as very good, in 53% as average, and in 21% as below average. Thus over three-quarters of the mothers were good women doing a very creditable job in bringing up their families and caring for their children. A few of the mothers could be called negligent or indifferent. Six mothers regularly left a substance which they knew to be dangerous within easy reach of their children, and three continued to do so after the child had been poisoned. Most mothers had a reasonable appreciation of the dangers of poisonous substances to their children, and kept these substances in a position which they considered to be safe from their children's reach. However, 27% of mothers whose children had obtained the substance in their own homes, were not aware that the product which the child took was actually poisonous. The majority of these substances were common household cleaning preparations, particularly one brand of furniture polish. None was bottled or labelled in any way to indicate that it was poisonous. Probably owing to the fact that most patients were under two years of age, the mothers usually knew within minutes that a substance had been taken. It was rare for a child to have been out of his mother's sight for as long as fifteen minutes or more.

Type of Child Who Took Poison.

The children who took poison could be classified into three groups, those who took it spontaneously (131 cases), those who were given it by another child (15 cases), and those who obtained it by accident (nine cases). An impression was formed that the majority of children who spontaneously took poison had certain characteristics which made them appear different from the average child. As a group, they appeared to be intelligent, very active and mischievous children. Many had walked and climbed at an early age and had no fear of heights. Most were exceptionally curious and poked into cupboards and drawers, and liked to find out how things worked. Mothers frequently stated that these children acted on a level above that of their age. When asked how the child compared with older brothers or sisters at the same age, mothers frequently said with feeling: "Oh, this one is a real villain", or "I never know what he will do next". On the whole, mothers seemed to be aware of the characteristics of these children and expected "anything to happen". Pica was a common characteristic. In the younger child, taking a poison appeared to be associated with imitation of a recently observed act, such as drinking out of a bottle or taking pills, or with repetition of a new activity, such as learning to drink unaided. The fact that 22% of the children had swallowed a poisonous substance on more than one occasion suggests a child with unusual curiosity.

Six children who took poison spontaneously exhibited several characteristics which were different from the remainder of the group. Two habitually wandered, two frequently lit fires, and two were mentally retarded after encephalitis.

By contrast, the fifteen children who swallowed a substance at the invitation of another child were frequently described by their mothers as being timid or shy and easily led. They were a little older than the majority of children who took poison spontaneously, and their mothers, as a group, were not as alert mentally as the other mothers. Several of these children had previously been victims of the same child.

Nine children swallowed the poison by accident; three were given it by their mothers in mistake for a medicine, three older children were experimenting, and the remaining three took it in unavoidable circumstances. These children appeared to be normal, average children.

Circumstances of the Poisoning.

These 155 children swallowed a wide variety of poisons, taken from an equally wide assortment of places. There did not appear to be any relationship to day of the week, but during the hot summer months—December, January and February—there was a slight rise in cases treated and a noticeable increase in the proportion of fluids swallowed.

Medicaments were the most common group of substances taken, and 62% were in tablet form. Of all medicaments taken, half were either sugar or chocolate coated tablets, flavoured medicines or attractively coloured substances.

Accessibility of the poisonous substance to the child was of considerable importance, for in 47% of cases the substance was readily obtainable, though not always in sight.

In 25% of these cases the product was actually in use, usually by the father. Of children who climbed to obtain a substance, 28% took it from a position considered to be out of the reach of a child of that particular age. These substances were all taken from a position higher than table level with as many from a high cupboard as were in sight on high shelves. The children in this group were slightly older than those who obtained things without climbing, 53% being over two years of age.

Nine and a half *per centum* obtained the substance outside their own homes, usually when accompanying their parents to visit friends and relatives who had no young children of their own. In nearly every case the substance was readily accessible, and often the child swallowed it within minutes of arriving at the place. A small number of these children were away from their parents either for holidays or on account of illness of the mother.

In 9·5% the substance was given by other older children, most of whom did not taste it themselves. However, if the other child climbed to obtain the product, he was usually involved. The majority of these cases happened in the patient's home.

A very small group of patients (nine of the 155) were considered to have swallowed the product entirely by accident. Three children were given a poison accidentally by the mother in mistake for a medicine. All three mothers were experiencing considerable mental strain at the time, and the circumstances indicated that they were not careless. Three older children were experimenting and the remaining three obtained the poison in varied but entirely accidental ways.

In a few cases the child obtained tablets or a fluid from a rubbish tin where the mother or a neighbour had placed them for safe disposal.

Storage.

In the 155 homes visited the pattern for storage of medicines and household products was fairly standard. Medicines were usually kept in the bathroom cabinet or the highest kitchen cupboard. Occasionally the top of the mother's wardrobe or linen press was used. Household cleansers were mainly kept on a high laundry shelf or in a low kitchen cupboard, depending on the mother's awareness of potential danger. Kerosene and other products likely to be used by the father were kept in the laundry, shed or garage. It was much more common for the garage or shed door to be locked than the medicine cupboard. Only eight families kept drugs in a locked cupboard, and only four families of 155 kept all medicines and all household substances under lock and key. It is important to note that at the time of poisoning 60% of the products were out of their usual place, either because they were being used or because they had been used in the previous twenty-four hours. In the latter case it was usually a medicine used during the night for a sick child. Of the substances, 25% were not in the original containers. These were mainly kerosene and petrol, which had been placed in open tins and beer, cordial or sauce bottles to facilitate use. Most of these substances were actually in use at the time the children swallowed them.

Labelling of Poisons.

In discussions on the handling of all poisons in the home it was apparent that most mothers regarded medicines as dangerous. With other products they were frequently guided by the presence of a poison label or by a distinctive shape or colour of the bottle. Of the mothers whose children had obtained the substance in their own homes, 27% did not know that the product was dangerous, though they did not necessarily always leave it accessible to a small child. Most said "the label didn't say so" or "the doctor didn't tell me".

Discussion.

Poisoning is a common accident among children, especially in those aged one to three years. In Melbourne during 1954 the incidence was approximately one in 130 children between the ages of one year and three years. This estimate was made from the total number of children aged one to three years treated at all hospitals in Melbourne and the child population of this age group. Obviously some children will be treated by their family doctor, but this number is probably small.

This accident causes considerable distress to parents, as frequently they feel that they have been negligent in allowing their child to get at poison. Several authors—Ross and Brown (1951), Fraser (1954), Foley, Dreyer, Soule and Woll (1954), and Dennis and Kaiser (1954)—have attributed the high incidence of accidental poisoning as being chiefly due to carelessness or negligence of parents. These opinions have apparently been expressed without adequate investigation of the social background of the home and circumstances of the poisoning, for no data are given on which these opinions are based.

The present study clearly indicates that 79% of the mothers were careful, conscientious women who looked after their children well. The standard of mother care corresponded well with social grading and home standards. Of the children, 79% came from the professional, business and skilled trade classes, and 63% of the homes were a good standard. In only 16% were homes substandard, dirty and without adequate facilities for a decent standard of living.

The unexpected social distribution of accidental poisoning as revealed in this survey might possibly be explained in two ways: first, that the 155 homes studied were not a representative sample of the homes of all children poisoned, and second, that mothers from the economically and socially inferior homes did not seek medical advice. The first explanation is most unlikely, for the Royal Children's Hospital treats approximately 80% of all children accidentally poisoned in Melbourne. Furthermore, the homes studied were selected at random, and the suburban distribution of the 155 homes corresponds closely to the suburban distribution of the total 419 homes. The second opinion is highly improbable, as mothers from poor or slum areas are rarely indifferent to any threat of their children's well-being. It was also found that these mothers brought their children to hospital just as promptly as those from good homes.

The conclusion from this study is that accidental poisoning is not commonly associated with poor housing conditions, overcrowding and a poor or indifferent standard of maternal care. Seiler and Ramsay (1954) in a survey of all accidents to children in the home remark that poisoning did not seem to be associated with substandard homes and overcrowding, as was the case with burns and scalds.

How, then, with good parents, and in good standard home conditions, do these accidents occur? The circumstances of many of the accidents suggest that if the parents had known more, the accidents would not have occurred. Three factors stand out in this study as being of major importance in the majority of cases of poisoning: first, the availability of the substance taken; second, the knowledge of the mother with regard to the poisonous substance; and third, the type of child poisoned. The following facts on the availability of poisonous substances to children are very significant. In 47% of the cases occurring in the child's home the poison taken was readily accessible, and in 60% the substance either was being used or had been in recent use. In only eight homes were drugs kept in locked cupboards, although they were usually kept in a reasonably high cupboard or on a high shelf. Often the poison taken was not in its proper container, and this was frequently so with petroleum products, which were a common group of substances taken.

Secondly, in 27% of cases the parents were unaware that the substance taken was dangerous to the child. The manufacturer of common household preparations frequently eulogizes his preparations by saying they are harmless and safe. Lavatory cleaner and furniture polish are doubtless safe and harmless for their designed purpose, but not for ingestion by the two-year-old.

Thirdly, is the child who spontaneously takes poison different from his fellows? A large number of these

children were of the active exploring type, whose behaviour was frequently unpredictable and who showed considerable initiative. The mother was often aware that this child was different from her other children. The observation that the child so often took a drug or other substance while it was being used or soon after its use may well be accounted for by the interest which something new arouses in the curious child. It is possible that these children may be different from the average child. Certainly this point merits further investigation.

Prevention.

The fact that so many of the cases of accidental poisoning occur in good homes, with good mothers of average or above average intelligence who are economically secure should mean that with education, prevention of many of these accidents is possible. Parents should be aware of the frequency with which toddlers, aged one to three years, ingest new substances and also of the necessity to store safely at all times drugs, household preparations and any other substances which are poisonous. Parents should know that there is a special risk for the inquisitive, exploring type of child in the age group one to three years, and that extra precaution for his safety is necessary. All drugs must be kept in a locked cupboard or at least on a shelf so high that even a very active child cannot possibly reach them. As soon as a drug is used it must be restored to its proper safe place. Under no circumstances should it be left lying about, as it will often excite the interest of the curious child. Similarly, household substances for use both in and outside the house should be in proper containers and stored in safe places out of the reach of children.

These are sound counsels to prevent poisoning, but how shall they be implemented? Education of the parents who are responsible for both protecting and teaching the child is the key. It is probably best carried out through two main channels, the personal trusted home adviser and propaganda. Home advice is best given by the health visitor or nurse, who can see the home at first hand and advise the mother on the spot. Dr. Deem (1955) has personally advised us that this practice is carried out in New Zealand, where Plunket nurses have special training in accident prevention. They inspect where drugs and other poisonous substances are stored and so can warn the mother if she is at fault. Mothers are responsive to this advice. Mothers' clubs, infant welfare clinics and kindergartens can play their part in giving advice and in staging demonstrations and talks on child care and accident prevention, but primarily education will be best given in the home. The family doctor can help by suitable advice at the right time, and the pharmacist can always give warnings on the dangers of drugs to young children.

One doubts very much the widsdom of any mass wireless or Press propaganda such as is in common use to sell soap or health tonics. One does not learn to care for a child by listening to the wireless or reading a newspaper. Care can be learnt only from a trusted, experienced adviser personally giving advice or discussing a worry or problem.

Legislation can play an important part, and all drugs and any substance which is poisonous and in common use in the home should bear a label: "Dangerous to young children. Store safely out of reach." A label such as this should be acceptable to manufacturers. Most if not all poisons are satisfactorily dealt with by the *Poisons Act* as far as adequate control of both wholesale and retail sales is concerned, but legislation does not advise the purchaser of the danger to young children.

Many of the social data and the risk of accidental poisoning are now known. Measures to reduce the risk of poisoning are straightforward, and it is up to pædiatricians and infant welfare workers and organizations interested in child care to implement them.

Summary.

1. Poisoning is a relatively common accident in young children, especially between the ages of one and three years. At least one child in every 130 children between the ages of one and three years takes a poisonous substance.

2. These accidents are very distressing to parents, who frequently feel that they have been careless or neglectful.

3. Negligence or carelessness on the part of the parents is an uncommon cause of poisoning; 79% of the mothers are good and careful, and handle their children well.

4. Sixty-three *per centum* of the children come from good standard homes, and 79% of the fathers are professional or business men or skilled tradesmen. The smaller number come from the poorer families who belong to the labouring or semi-skilled groups and who have a lower material standard of living.

5. Three important factors relevant to prevention emerge from this social study: first, the larger number of children who take poison are active, curious children; second, many of the substances ingested are readily accessible to these children; and third, it is not realized by parents that a number of common household substances are dangerous.

6. Prevention of a considerable number of accidental poisonings will probably best be achieved by (*a*) education of the parents as to the frequency and danger of poisoning for the child of one to three years of age, especially for the inquisitive child; (*b*) suitable storage of all poisonous substances; (*c*) suitable labelling on all poisonous substances; (*d*) education which will probably be best carried out personally, preferably by a visiting nurse and family doctor.

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ACCIDENTAL POISONING IN CHILDHOOD.[1]

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DURING the ten months ending March, 1955, 59 patients suffering from accidental poisoning were brought to the casualty department of the Royal Alexandra Hospital for Children. This is but a small fraction of the total number of cases in Sydney during this period, since most such patients are treated in district hospitals.

Much of the study of these patients overlaps and confirms the Melbourne investigation undertaken by Miss

[1] Read at a round table conference on accidental poisoning in childhood at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

Allan and Dr. Williams, and it is not intended to record such results in this paper. There are, however, some truly clinical aspects of accidental poisoning which are important when prevention is being planned.

Delay in Seeking Medical Treatment.

The first of these clinical matters is the interval from the moment when the child ingests a foreign substance to the time at which he is presented to a doctor for treatment. This has to be divided into two periods: the first is from the time of ingestion to the moment when the parents recognize that the child has taken a foreign substance, and the second is from this point at which recognition occurs to the time when the child is presented for treatment.

Table I depicts the first of these periods. It is clear that recognition is almost immediate in more than three-quarters of the cases, but it can also be seen that in a few cases recognition is considerably delayed. Several of the patients developed symptoms and were presented to a doctor or to the Casualty Service where a diagnosis of poisoning was made; the parents then sought and found evidence that a poison had been taken.

TABLE I.

Time Interval from Ingestion to Recognition.

Time Interval.	Number of Patients.
0 to 15 minutes	46
15 to 60 minutes	6
1 to 2 hours	1
Over 2 hours	6

Most children are brought to a doctor for treatment within one hour of their mothers' becoming aware that a foreign substance has been taken (see Table II). It is significant, I think, that approximately one-third of these children are not brought for treatment until more than one hour has elapsed after such recognition.

TABLE II.

Time Interval from Recognition to Presentation.

Time Interval.	Number of Patients.
0 to 30 minutes	31
30 to 60 minutes	7
1 to 2 hours	17
Over 2 hours	4

It can be seen in Table III that for most patients this delay was due to the fact that the parents were unaware of the toxic nature of the substance taken until a neighbour or friend informed them. A few parents, although aware of the possible hazards, waited to see if any toxic symptoms resulted. This attitude contrasted sharply with the anxiety and sense of urgency shown by most parents.

TABLE III.

Reason for Delay in Presentation.	Number of Patients.
Distance from hospital and transport difficulties	4
Lack of awareness of poisonous nature of substance taken ..	12
Waiting for symptoms to develop	5

Severity of Illness Resulting from Accidental Poisoning.

Of the 59 children seen in the Casualty Department of the Royal Alexandra Hospital for Children during the ten months to which I referred, only nine developed symptoms and none died. During a three-year period ending December, 1954, 92 patients were admitted to this hospital because of accidental poisoning.

That these children were admitted to hospital suggests either that they had symptoms at the time of admission or that the admitting officer suspected that symptoms would develop. Table IV shows that a large number of these admitted patients did not develop any symptoms, and that approximately one child in every eight admitted had a dangerous or fatal illness.

TABLE IV.

Severity.	Number of Patients.
No symptoms	40
Mild or moderate illness ..	41
Dangerous illness	7
Death	4

In searching for reasons for severity, it did not appear that factors in the child, such as age or delay in treatment, were significant. It was clear that many patients with dangerous or fatal illness had taken internal medicaments (see Table V).

TABLE V.

Nature of Poison and Severity.

Nature of Poison.	Number of Cases.	Dangerously Ill.	Died.
Kerosene and related substances ..	26	0	0
Pesticides and weedicides	14	2	1
Purgatives	2	0	0
Salicylates	3	0	0
Caustic soda	1	1	0
Ferrous sulphate	2	1	1
Digitalis	3	2	1
Antihistamines	5	0	1
Total	92	7	4

I have not attempted in Table V to make a complete list of poisonous agents taken by children. I have listed certain poisons which have seemed of outstanding importance because of the frequency with which they are taken, because of the parents' lack of awareness of the danger involved, or because of the outstanding danger of the agent itself in the amount usually taken by children.

1. Kerosene is frequently taken by children, and although almost half of these patients developed pneumonia, none had a serious or fatal illness.

2. Weedicides and pesticides are not only taken frequently, they also account for a significant proportion of serious and fatal cases.

3. Purgatives and salicylates are frequently taken by children without their parents' knowledge. Very few such patients develop an illness severe enough to warrant admission to hospital, and none of these patients had a dangerous or fatal illness.

4. Caustics and corrosives are now taken very seldom by children in Sydney; when they are taken, a serious illness is the usual result.

5. Certain pills and tablets cause serious and fatal illness. These are ferrous sulphate, digitalis, "Benzedrine", the antihistamines and some travel-sickness remedies. Fortunately these drugs are not taken very frequently by children.

Reaction of Parents.

The final clinical observation is not the least important. The parents of these children carry a load of grief and guilt and regret which is greater than with any other illness except perhaps diphtheria. In planning a campaign of prevention, let us try not to add to this burden.

Prevention.

The attitude of the clinician to the prevention of accidental poisoning is influenced by what he sees of poisoning as a clinical entity. His attention is focused on those poisons which children take frequently and those which cause severe and fatal illness.

I think all would agree that the first step is a programme to educate parents in the dangers of certain chemical agents. I believe that such a programme should, when first started, be directed to a few poisons only. A short list of poisons of outstanding importance will be different in various parts of Australia. The list I suggest for Sydney consists of: (*a*) kerosene; (*b*) weedicides and pesticides; (*c*) certain pills and tablets, including ferrous sulphate, digitalis, antihistamines, "Benzedrine" and travel-sickness remedies.

Although ingestion or inhalation of kerosene rarely causes dangerous illness, a high percentage of affected patients develop paraffin pneumonia. Moreover, it is the commonest poison, and many parents are unaware of its dangers. Weedicides and pesticides are also frequently taken, despite the fact that a high proportion of parents are aware of their danger to young children; these agents account for an appreciable number of the serious and fatal illnesses due to accidental poisoning. Not a great many children take the pills and tablets I have listed, and in view of their serious effects, it is well that the numbers are small. Parents do not seem to be aware of the dangers of this particular group.

I would not include purgatives, salicylates, sedative drugs, caustics and corrosives. Purgatives and salicylates have not caused enough severe illnesses to warrant inclusion, although parents are still not aware of the possible dangers of these drugs; they may need inclusion later. Sedative drugs are taken less frequently than purgatives and salicylates, but sometimes cause serious illness. Parents are aware of the hazard, and a programme of propaganda directed at other agents will intensify, rather than reduce, this awareness. Parents are fully alive to the terrible consequences of taking caustics and corrosives. When these agents are taken it is usually due to extraordinary circumstances causing a temporary lapse in stringent precautions.

The list I have suggested is based on Sydney experience, and it is only reasonable to assume that in other cities a different list would be necessary. In Melbourne, for example, a certain brand of furniture polish would deserve almost as much attention as kerosene.

There are many ways in which a publicity campaign, aimed at these agents, could be started immediately. An occasional reference to a single poison such as digitalis in the writings of medical people in the lay Press and in women's magazines would be of great benefit. A paragraph referring to the dangers of an agent such as ferrous sulphate could be placed in one of the popular "columns" of a daily newspaper. These columns are widely read and such propaganda would have a good effect. At present, the Royal Alexandra Hospital for Children is preparing a booklet aimed at prevention of accidents in children, and discussing their first-aid management. The value of such a booklet is no doubt somewhat limited. The highest incidence of poisoning at our hospital last year was in the month following the Health Week Exhibition at the Town Hall. A booklet issued at that time contained an article of mine on the prevention of accidental poisoning in childhood. I have no doubt that the oil companies will cooperate, if approached, in an endeavour to inform parents of the possible dangers of kerosene. Most parents are not aware of the toxic effect of kerosene, and if they were, it would not be left so accessible to small children.

On the level of personal instruction, I think it possible that pharmacists might inform parents that certain drugs collected from their pharmacies are dangerous to small children. They would be likely to do this only if the list of agents was kept reasonably short. The general practitioner visiting patients in the home is in an excellent position for giving personal advice on the possibilities of accidental poisoning. It would be necessary to convince him of the frequency and gravity of this problem before he would cooperate. It may be difficult to convince him of this when other, more easily preventible diseases are so common in the Royal Alexandra Hospital for Children. Infantile scurvy is twice as common as kerosene pneumonia, and tetanus causes twice as many deaths as the whole of accidental poisoning.

In spite of any campaign for prevention, some patients will continue to suffer from accidental poisoning. A practical suggestion, therefore, is the establishment of a Poison Information Bureau. Such a bureau would be most valuable if established at the principal children's hospital in each State capital city. One of its functions would be to provide information to parents and practitioners by a twenty-four hour telephone service at registrar level. This information should include: (*a*) the formulæ of patent and proprietary drugs; (*b*) the formulæ of household cleansers, solvents, pesticides and so on; (*c*) toxic effects of these substances; (*d*) minimum toxic doses in relation to age or body weight; (*e*) new antidotes and methods of using them. The bureau would also collect statistical information on the incidence of various types of poisonings, effects of these poisons, and results of various methods of treatment.

In conclusion, it has been demonstrated that the incidence of accidental poisoning is rising. In the house of tomorrow there will be an increasing number of chemicals for use by the housewife and the home gardener, and consequently an increasing chemical hazard for the young child. It would seem reasonable to plan, now, for a reduction in the incidence of accidental poisoning before it climbs still higher.

SOME ASPECTS OF DIABETES MELLITUS IN CHILDHOOD.[1]

By S. E. J. ROBERTSON,
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DURING the last two years, 46 children under the age of thirteen years have been attending the Diabetic Clinic at the Royal Alexandra Hospital for Children. The purpose of this paper is to mention briefly certain conclusions that have been arrived at from the study of these children.

Of these children, 16 are male and 30 female. The youngest child at diagnosis was ten months of age, and five were found in the first two years of life. The big incidence occurred in the fifth year, when the diagnosis was made in 15 children.

I should like to confine my remarks in the remainder of this paper to the natural history of untreated and treated diabetes in childhood, and to certain aspects of treatment.

The cardinal features of *diabetes mellitus* in children are excessive thirst and polyuria. These two symptoms are always present. The longest duration of these symptoms was two months, and the shortest was three days. Excessive appetite is rarely remarked on by the parents, the appetite usually being poor. Symptoms often seen in adults, such as boils or pruritus, are not found in children. Without treatment the disease is rapidly progressive and ketosis will supervene, often within a few weeks. The child becomes tired and irritable and, with the appearance of drowsiness and vomiting, coma with air hunger and acetone on the breath is only a matter of hours. The point I should like to make at this stage is that thirst, polyuria and glycosuria mean diabetes in a child, and treatment should begin at once. An immediate blood sugar content estimation figure is always over 200 milligrammes *per centum* and usually over 400 milligrammes *per centum*. In no case in this series was *diabetes mellitus* detected by means of a glucose tolerance test instituted because of the lone finding of glycosuria without thirst or polyuria.

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

I feel that if a child has thirst, polyuria and glycosuria, diabetes is always present. The only confirmatory test is an immediate blood sugar examination, and the carrying out of a glucose tolerance test only wastes valuable time. Conversely, the performance of a glucose tolerance test on a child with glycosuria, without thirst or polyuria, may be of theoretical interest, but in my experience it has never detected *diabetes mellitus*.

Mistaken diagnosis in the earlier stages results from failure to test the urine for sugar, the most common misdiagnosis being functional enuresis, cystitis or nervous polyuria. When vomiting or drowsiness appears in the later stages, diagnoses of an acute abdominal crisis or meningitis may be made because of the rigid abdomen or stiff neck so often found with ketosis. From the rapidity with which symptoms are seen to get worse in untreated *diabetes mellitus* in childhood, it is evident that sugar tolerance rapidly disappears. If, after the initial diagnosis, treatment is energetic, sugar tolerance returns almost to normal, and the child may remain free of urinary sugar with very little or no insulin, providing he has little carbohydrate in his diet, is emotionally stable and has no intercurrent illness. However, the need for exogenous insulin inevitably recurs; within three to six months the child has to have insulin injected daily, and this need continues permanently. As the child grows, the daily insulin requirement increases and may be very much greater than that necessary to maintain an adult whose pancreas has been removed. The precise reason for this is a matter of argument, but the most reasonable explanations are that an anti-insulin hormone is produced or that increased production of the growth hormone of the anterior pituitary gland occurs and antagonizes the hypoglycæmic action of insulin. Emotional strain, chronic infection and particularly puberty increase the need for insulin in children.

These patients have all been examined regularly for evidence of vascular degeneration. No changes in the retinal vessels, albuminuria or hypertension have been observed. One patient, whose onset occurred at the age of twenty-one months, has always presented a severe behaviour problem and is now a ward of the Child Welfare Department. He has been admitted to hospital on 21 occasions in acidosis in his ten years of diabetes. Despite this he has no evidence of vascular degeneration. There are insufficient patients in this series who have been examined after ten years of diabetes to justify the statement that vascular complications do not occur in children, but they must be exceedingly rare.

During the last two years no child regularly attending has had to be admitted to hospital with acidosis and dehydration sufficiently severe to require intravenous therapy. Experience in the management of diabetic coma has been limited to those patients in whom this complication has been present on diagnosis. The initial dose of ordinary insulin in diabetic coma should be adequate and should not need to be repeated for six hours. Doses of insulin repeated at shorter intervals than this are likely to have a cumulative effect, with the occurrence of hypoglycæmia as the patient recovers. Two units of insulin per kilogram of body weight are usually sufficient as an initial dose. Blood sugar estimations should be repeated at three-hourly intervals in the early stages and the next dose is estimated by the change in blood sugar content in the first six hours. Urine specimens, in the absence of blood sugar estimations, can be used to assess the efficiency of treatment, but should be obtained from an indwelling catheter. By this means a specimen tested shows the amount of sugar present in urine recently secreted by the kidney. Fluids given intravenously to relieve dehydration should be very generous as the deficit from polyuria and vomiting is often exceedingly high. Isotonic saline is given repeatedly at first, followed by 3·75% glucose in one-quarter isotonic saline. Glucose solutions have not been used until a blood sugar level has fallen to 200 milligrammes *per centum*, which usually occurs in about six hours. Potassium salts to give the normal daily requirement of the child are added to the initial infusion, unless anuria is present —the last being exceedingly rare in children. Alkali, in the form of molar sodium bicarbonate, is added to the initial infusion, the amount depending on the level of serum bicarbonate. Recently fructose, in 5% solution, has been mixed with an equal quantity of isotonic saline and this has been used as the original infusion to which potassium salts and sodium bicarbonate have been added. This proved very satisfactory, the blood sugar falling at a fast rate under the influence of insulin.

Once the dehydration and ketonuria have been relieved, usually in twelve to twenty-four hours, the patient is given a fluid diet and ordinary insulin, each divided into four equal parts and given six-hourly. Diet prescribed is 1000 Calories *plus* 100 Calories for each year of age. The carbohydrate content provides 50% of the Calories, and to this is added protein of 2·0 grammes per pound weight for children under the age of five years and 1·0 gramme per pound weight for those over this age. The balance of the Calories is made up by fat. Usually the patient can take solid foods after forty-eight hours. Urine specimens are tested every six hours and the insulin dosage is adjusted accordingly. The adjustments of insulin will depend on the sensitivity of the blood sugar to insulin in each individual case, and this can be assessed after the first few doses.

As soon as blue or green results to the Benedict's test appear, the patient is given ordinary insulin three times a day, and two days later a longer acting insulin is given once a day. The diet is increased according to appetite, the same proportions of carbohydrate, protein and fat being maintained.

Insulin dosage is regulated by urine tests performed before meals. The urines tested must be what are called "second" specimens. The bladder is emptied and the urine discarded half an hour prior to the collection of the specimen which is to be tested. Usually a child has no difficulty in doing this after a little practice. Blood sugar control estimations being made every six hours for twenty-four hours are of interest, but satisfactory control can be obtained without them.

Satisfactory control of the diabetic child in hospital bears no relationship to control in the home, and as soon as the child is well he should be discharged home to be seen in the out-patient department at weekly intervals. Parents are instructed in the measuring and giving of insulin, in the testing of specimens of urine for sugar and acetone and in the recording of the results, and in the weighing of the diet. As mentioned above, the child's exogenous insulin requirements diminish almost to zero after energetic treatment at the onset. Also, the child is much more active at home than he is in hospital. For these two reasons it is wise to reduce insulin until urinary sugar is heavy before discharging the patient from hospital. If this is not done, readmission of the patient in hypoglycæmia is likely in twenty-four to forty-eight hours.

Success in the management of the child as an out-patient depends, as in the management of most chronic diseases of childhood, on the parents. Most success will be gained with a mother who is intelligent enough to learn about the disease and to adjust insulin dosage and diet when upsets occur, who is conscientious in the routines of injections and diet, who is strong willed in enforcing the necessary dietary and injection discipline and, lastly, who has sufficient strength of character to allow the child to live a normal full life, apart from the necessary dietary restrictions and injections. A stupid but conscientious mother can be taught, and an over-anxious, worrying mother, if well managed, will eventually obtain confidence, but the careless mother who will not try to understand and carry out instructions, will make successful control difficult and sometimes impossible.

It is essential to realize that the child's insulin requirements vary from day to day and must be altered frequently. Adjustment of the dose by the doctor at monthly or even fortnightly intervals leads to poor control. It is best to train the mother to alter insulin dosage according to urine tests. So as not to make a fetish of urine testing, two specimens are examined daily; a "second" specimen before breakfast and a "second" speci-

men before the evening meal. The aim of treatment has been to have a trace of sugar in these two specimens.

At the beginning of the period of observation of these patients, almost all were having two daily doses of ordinary insulin. This was an easy method of controlling any diabetic, but to render the urine almost sugar free before the evening meal and before breakfast needs such a dose that hypoglycæmia is likely before lunch or about midnight.

Protamine zinc insulin alone was found to produce quite unsatisfactory control. Protamine zinc and ordinary insulin mixtures were found to be occasionally successful, but too unpredictable, and frequent variation in dosage was also difficult. The injection of protamine zinc and ordinary insulin separately before breakfast was successful in a few cases, but as a rule was too cumbersome and without the necessary elasticity. The grave disadvantage of protamine zinc insulin, as far as diabetic children are concerned, is that hypoglycæmia, when it occurs, tends to be severe, prolonged and hard to relieve. Mainly for this last reason, protamine zinc insulin has been abandoned in this clinic.

Globin zinc insulin, as a single morning dose, has to be so increased to avoid early morning glycosuria that hypoglycæmia tends to occur in the late afternoon. However, if it was given twice daily, before breakfast and the evening meal, control was most satisfactory. As a rule the evening dose was two-thirds of the morning dose. Alterations in dosage were usually made by the parents according to the twice daily tests of "second" specimens. If two evening specimens in succession showed heavy sugar, the morning dose was increased by two units. If these two specimens showed no sugar, the morning dose was decreased by two units. The evening dose of insulin was regulated by the results of the morning tests in the same fashion. This system, easily followed by parents, produced excellent results and is still used with occasional patients. However, it entails twice daily injections, and hypoglycæmia, when it occurs, tends to be severe, although not so severe as that following the use of protamine zinc insulin.

In October, 1953, a supply of insulin zinc suspensions was received from the Novo Therapeutiske Laboratories of Copenhagen. These were tried on several patients and were found so successful that they are now used to control all except a few patients. These insulins are solutions of insulin crystals. The crystals are of two sizes; the smallest crystals, insulin zinc suspension (amorphous), have a duration of action of twelve hours; the largest crystals, insulin zinc suspension (crystalline), have a duration of action of thirty-six hours. If 30% of the former is mixed with 70% of the latter, a mixture is produced which acts steadily for about twenty-four hours and which is suitable for most patients.

As soon as the initial ketosis and hyperglycæmia have been controlled by multiple injections of ordinary insulin, and the child is having a normal diet, an equal number of units of insulin zinc suspension is given before breakfast as was formerly given during the entire day as ordinary insulin. The dose is then either increased or decreased according to simple rules. If an evening test and the following morning test show a red result to a Benedict's test, the dose is increased by two units. Also if four specimens in succession produce orange or red tests, the dose is increased by two units. If an evening and the following morning tests produce blue results with a Benedict's test, the dose is reduced by two units. If four tests in succession give blue and green results, the dose is also reduced by two units. With the use of this simple system, all but a small proportion of the children in this series have achieved good control, as assessed by the absence of anything more than occasional heavy glycosuria and very infrequent hypoglycæmia and by good general health, normal growth and the absence of complications of *diabetes mellitus*.

When a patient has been previously well controlled on two doses of globin zinc insulin or ordinary insulin, or on some combination of protamine zinc and ordinary insulin, the dose of insulin zinc suspension becomes 50% to 100% higher than the previous total dose of insulin used. This dose may approach one hundred units daily in puberty, but this is no disadvantage with insulin of eighty units to the cubic centimetre. In a few cases an increase in the dose of insulin zinc suspension has produced hypoglycæmia before satisfactory results with twice daily tests have been achieved. In these cases the addition of the slower acting insulin, zinc suspension (crystalline), then produces good control. This addition has been as high as 50% of the total dose. Insulin hypoglycæmia still occurs, but less frequently and less severely than with insulins previously used. Such reactions tend to be much slower in developing and allow the patient ample time to take a little carbohydrate or to advance the time of the next meal. When acute infections develop, the dosage is increased by 10% to 20%. If this increase does not prevent heavy glycosuria or ketonuria, ordinary insulin, 20% of the total dose, is given before meals in addition, if a "second" specimen before that meal shows heavy glycosuria.

Isophane insulin became available about the same time as insulin zinc suspension. It was used on one patient with excellent control. However, this patient has had her disease for only one year; and, as her requirement increases, she will probably do better on insulin zinc suspension. Globin zinc insulin, given twice daily, is still being used on two patients—a girl in puberty who could not be controlled on insulin zinc suspension and a boy who presents a severe behaviour problem. All patients in this series have a strictly prescribed diet. This is increased according to appetite, and no attempt is made to restrict the total Calories if obesity does not appear. It is hard to estimate what proportion of the patients keep strictly to their prescribed diet, but it is probable that most do, and the others do at least in a qualitative fashion. It is felt that the "free" diet advocated in Continental Europe would probably result in more glycosuria. Whether such glycosuria does any harm is still a matter of argument.

Owing to the fact that children prefer to have their insulin injected in certain localized areas which they know to be painless, subcutaneous fatty atrophy is a common and a difficult problem. It seems to occur just as often with insulin zinc suspensions as with other insulins, and the cause is quite unknown. If the area of atrophy is avoided the subcutaneous fat will return in one to two years. The prevention consists of never injecting insulin in the one place more often than once a month.

Hypoglycæmia, to a mild degree, is almost unavoidable in any well controlled diabetic child. It can usually be prevented by avoiding late meals and by giving extra food before and after unusual exercise. Severe hypoglycæmia is extremely dangerous to the central nervous tissue of children and must be avoided at all costs. In this series there are two children with severe *grand mal* epilepsy and frequent "akinetic" turns, of which the latter have so far proved resistant to all treatment. Both children have gross abnormalities in their electroencephalogram, not related to their blood sugar level, and in both cases the epilepsy followed severe hypoglycæmia brought about by overdosage of protamine zinc insulin. One of these patients developed precocious puberty in addition, which is thought to be due to damage to the hypothalamus from hypoglycæmia.

Summary.

A series of patients in a diabetic clinic in a large children's hospital have been studied for a period of two years. A brief summary of the management of diabetic coma is made. Methods of bringing the child under control and maintaining this state by means of insulin and diet are discussed. It is emphasized that day to day alterations in insulin doses are necessary for successful control of diabetes in children, and this is best obtained by education of the parents. Various forms of insulin therapy have been tried, and it has been found that the most successful results have been obtained by the use of insulin zinc suspensions. Brief mention is made of insulin atrophy and the necessity for avoiding severe hypoglycæmia in children.

THE SYNDROME IN THE INFANT RESULTING FROM MATERNAL EMOTIONAL TENSION DURING PREGNANCY.[1]

By ELIZABETH K. TURNER,
Melbourne.

THE syndrome to which I refer is well known. The infant manifests from birth increased restlessness and fussiness, excess crying and irritability, vomits considerably, and frequently has loose stools; it generally sleeps less than other infants, and shows unnatural sensitivity to sound, starting violently and often crying loudly.

This syndrome has been described under various names. Haas (1918) called the condition "congenital hypertonicity", as it was characterized by hypertonicity of all the skeletal muscles, and increased activity of smooth muscle of the gut associated with psychic irritability, expressed in insomnia, general restlessness and crying. Haas considered that the symptoms were due to increased vagal tone and could sometimes be diminished by the use of atropine. This concept is closely allied to the vagotonia discussed by Eppinger and Hess in 1915. They postulated that the central nervous system was abnormally sensitive and that minimal stimuli, usually without effect, led in some infants to marked irritative phenomena.

Jorup (1952) presented a most detailed and comprehensive study under the heading "Colonic Hyperperistalsis in Neurolabile Infants" and concluded that the symptoms were only slightly altered by drugs, changes of diet or environment, and that a constitutional factor was responsible.

Various other authors have described the same fussy, irritable, dyspeptic neonate by such adjectives as hyperkinetic, hyperactive, or suffering from vagogenic enterospasm. The ætiology has been variously ascribed to such factors as congenital imbalance of the autonomic nervous system, gastro-intestinal allergy, hereditary or constitutional, and cerebral birth injury (Lippman, 1928).

Certain normally delivered infants, nursed in ordinary full-term infants' nurseries, exhibited these symptoms in the first week of life, whilst others did not; these facts suggested that birth trauma and postnatal environment had no ætiological significance, and that the cause must be hereditary or constitutional or due to factors in the prenatal environment.

My attention was directed towards the possibility of the importance of the prenatal environment by a remark made by one of the sisters in charge of a nursery, who asked why they experienced such difficulty establishing "adoption babies" on their feeding formulæ, when they had, as a rule, so little trouble with the average baby.

I inquired from sisters in charge of the other nurseries and discovered that it was an unexpressed though generally accepted fact that babies for adoption quite commonly gave more trouble than other babies, and that they often showed an increased tendency to vomit and to be "difficult" with their feeds, and were frequently restless and required sedation.

I then had the opportunity to observe a number of mothers of illegitimate babies, to watch the behaviour of these babies separated from them at birth and kept in the nursery, and to watch their progress after adoption.

A number of these infants exhibited the symptoms just described, and some were dyspeptic and "difficult" for many months in spite of a placid and satisfactory environment with their adopted parents. I gained the impression that the worst of these were the offspring generally of the older and more anxious type of mother, who was more distressed during the pregnancy.

Further, I observed so many infants of the difficult hyperactive and restless type, born into otherwise normal families, whose mothers repeatedly inquired if their infants' behaviour could be caused by undue emotional stress which they had suffered during the pregnancy, that the conclusion was gradually and unwillingly forced upon my consciousness that prenatal emotional stress might affect the reactivity of the fœtal nervous system and alter the whole pattern of postnatal behaviour.

It is established that fœtal environment may play a part in determining characteristics of the physiological behaviour of the newborn, and that such things as maternal nutrition, oxygen tension and endocrine status are immensely important in preparing the fœtus to be adequately equipped for all the vital processes of his post-natal life. The placenta acts as a filter, allowing all particles of small enough size to pass; hormones may do this so that the maternal fœtal circulation becomes a common endocrine pool. Fœtal and maternal endocrine systems are complementary to each other; for instance, we are aware that the infant of a diabetic mother is likely to have hypertrophied islets of Langerhans, and to tend to secrete too much insulin in the first few days of life; and that the infant of a mother taking thyroid-suppressive drugs during pregnancy is likely to develop a compensatory goitre; obviously maternal hormones can reach and influence the fœtus.

Furthermore, endocrine organs have been shown to be basically end organs of the higher brain; acting through the hypothalamus and both lobes of the pituitary gland, emotional stress can profoundly alter the hormonal balance of the body; such well-established phenomena as the so-called "hypothalamic amenorrhœa" when suppression of the menses occurs because of emotional stresses, and pseudocyesis in which profound physical changes occur without physical cause demonstrate the effect of emotional states on the endocrine system.

Selye points out that emotional tension can act as any other stress agent, and affect the adaptive mechanisms of the body.

Mothers often state that after shock or fright the infant in the womb exhibits increased activity, amounting to the point of maternal discomfort in some cases, and for thousands of years it has been noted that maternal emotions can produce excessive fœtal movements. Saint Luke in Chapter I, verse 39 of his Gospel records that Elizabeth, the wife of Zacharias, after her sixth month of pregnancy, "heard the salutation of Mary, and the babe in her womb leaped for joy".

Whitehead in 1867 observed greatly increased fœtal movements during periods of maternal emotional stress and fatigue. Fatigue can cause an alteration in the oxygen and carbon dioxide levels of the blood as well as endocrine changes, and it has frequently been observed that maternal fatigue produces increased fœtal activity.

At this stage I was pleased to discover the work of a group of investigators at the Fels Institute of Human Development in Yellow Springs, Ohio, who had reached similar conclusions to my own, and who had backed these conclusions with some very convincing experimental work. One of these workers, Sontag by name, states that:

> Infants of mothers experiencing prolonged periods of severe anxiety during late pregnancy have been observed to be highly active and irritable with frequent bowel movements, and often with severe food intolerance.

He also states:

> Maternal emotions and severe fatigue may produce changes in the levels of some of the components of the mother's blood. Severe anxiety in the mother can produce a marked increase in muscular activity in her unborn baby.

In order to test the validity of the conclusions which had forced themselves upon me, I made a survey of 100 mothers and babies in the first seven to ten days of the puerperium at the Queen Victoria Memorial Hospital, Melbourne. I personally interviewed 30 mothers, and 70 other mothers filled in a *questionnaire* form. The latter method could be, I admit, subject to criticism, but it was all that was possible in the time at my disposal.

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

I then examined the babies whilst they were away from their mothers in the nurseries, being careful not to know their identification or history; the charge sister, who was generally unaware of the mother's marital status, gave me details of the infants' feeding and general behaviour. I eliminated from the survey all those babies whose feeding difficulties could be ascribed to physical causes, whether maternal or infantile, and all those whose irritability might be due to cerebral trauma or anoxia at birth.

Of the 100 surveyed, 71 mothers stated that they had no undue emotional stress during the pregnancy, and that they felt happy and contented throughout. They all produced normal babies who were not giving any difficulty. One mother with puerperal psychosis produced a normal baby.

Eighteen mothers stated that they had suffered with anxiety, worry or fatigue during the last few months of pregnancy. These worries ranged from such things as "worried whether the babe would be deformed", "trouble with mother-in-law", to "husband in hospital one month following a motor accident". All their babies behaved normally in the first week. Incidentally, the mother who said she worried whether the baby would be deformed produced a baby with a cleft-lip; there was no family history of the condition.

There were 13 difficult babies whose symptoms conformed to the syndrome described; of these mothers one was aggressive and hostile and refused to answer. She left the hospital "at-own-risk".

Six others stated that they had experienced no undue worries or fatigue; of these, on further investigation, three were found to have illegitimate babies, one of which later developed pyloric stenosis confirmed at operation. Two were new Australians having their first infants in their new land, one was Italian, and one Lithuanian. It would be impossible to say whether the hyperactivity in their babies might not have been genetically determined.

The other mother who said she had no worries said that her last baby had been illegitimate and later adopted, but that she had kept this absolutely secret from her husband.

Five of the 13 mothers of hyperactive babies admitted undue emotional stress or fatigue; these results are analysed in the accompanying table.

TABLE I.

Age.	Number of Children.	Baby's Symptoms.	Maternal Emotional State.
?	4	Excess crying, fussy and difficult with breast feeding.	First child twelve years ago illegitimate, then married and had two miscarriages; was extremely anxious throughout this pregnancy.
23	2	Vomiting and crying; required sedation.	Excessively tired and irritable during the last month of pregnancy. Baby kicked a lot *in utero* and kept mother awake.
19	1	Fought at the breast.	"Full of fears" in the last two months.
27	3	Vomiting required sedation.	Father suffered from war neurosis, threatened to desert twice during the last two months.
18	1	Crying excessively, sleepless and vomiting.	At first "worried over nothing in particular" but during the last stages became very anxious. Now it is all over, feels happy and contented.

On further inquiry from labour ward records, I discovered that there were no other illegitimate babies in the ward; in this survey the three illegitimate babies all behaved differently from the normal.

It is notoriously difficult to prove scientifically beyond doubt any postulate depending for its confirmation on human behaviour and emotions, and I suppose the survey which I performed proves nothing; but it does suggest to me that my impressions may have some justifiable basis and that further research along these lines may prove a fruitful field for the elucidation of some of the problems of infant behaviour which at present often baffle the pædiatrician.

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UNDESCENDED TESTIS: WHEN AND WHY TO OPERATE.[1]

By A. MURRAY CLARKE,
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IN spite of the fact that undescended testicles have been a problem interesting surgeons and pædiatricians since John Hunter's day, and countless papers have been written on the subject, it is still often a cause of bitter disputation. These heated arguments often exist primarily because of a failure to define terms clearly at the outset. For instance, the term "undescended testis" has been used in different ways. This afternoon in discussing when and why to operate, I am going to refer to all testes not in the scrotum at the time of inspection as "undescended", but will refer to one group as "true undescended".

A good illustration of the confusion that exists can be seen in the published health record of the Lady Gowrie Child Centres for 1940-1943, which shows an incidence of undescended testes ranging from 2·5% in Adelaide to 40% in Melbourne in similar children between the ages of two and five years.

Two points should be clearly made at the outset: (i) "Undescended testes" are four times as common in young boys as in young adults because 80% descend spontaneously. (ii) The 20% remaining are relatively few in number in the population, affecting 0·2% of the adult male population, or one in 500 males. When a patient presents, who on inspection has not his testicles in the scrotum, he must suffer from one of the following three types: retractile, ectopic, or true undescended testes. For a precise diagnosis, more than one careful examination is often necessary. The patient should be reclining comfortably and without apprehension, and the examiner with warm hands should gently palpate the area. Grasping at the testicle in the scrotum should be avoided, as this often makes the gonad disappear and it can slip into the abdomen and avoid detection. Success in finding an elusive gland is most likely if the hand is first placed in the iliac fossa cranial to the inguinal canal. On firmly stroking the area downwards in the line of the inguinal canal, a testis which cannot be felt may appear. Without releasing the tension of the stroking hand, and thus preventing the testis from disappearing again, the organ can be grasped between the finger and the thumb of the opposite hand and an

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

estimation can be made at the time of the length of the cord structures.

Further information including the presence of a hernia may sometimes be obtained by again examining the patient standing.

The Retractile Testis.

The retractile testicle lies above the pubes, sometimes in the inguinal canal, sometimes even in the abdomen, but most often in a large subcutaneous space, "the superficial inguinal pouch", to the outer side of the inguinal canal. Unless the patient is fat, the testis is here easily palpable. It may be pushed into the inguinal canal, when it usually becomes impalpable. It can be manipulated with more or less difficulty into the scrotum and the cord is found to be of normal length.

The Ectopic Testis.

The ectopic testis is easily felt and is almost always lateral to the inguinal canal, where it is often extremely mobile, depending on the length of the cord structures. The presence of a testis in a superficial inguinal pouch, even above and lateral to the external inguinal ring, does not necessarily mean that it is ectopic; a retractile testis can adopt that position.

The criterion of diagnosis is that, however mobile the testis may be, it cannot be made to enter the scrotum, where its way is barred by a fibrous mechanical obstruction.

If the testis is not felt in the inguinal region, the perineal, femoral and penile areas should be searched before assuming that one is dealing with an abdominal testis.

True Undescended Testis.

On examination, the true undescended type of testis may be felt in the normal line of descent of the testis, and by an acquired trick of manipulation may be made to enter the neck of the scrotum, showing that there is no mechanical barrier to descent. Short cord structures can be demonstrated by this manipulation at the same time.

It is impossible to tell by examination whether this testicle will later spontaneously enter the scrotum or whether if left it will remain imperfectly descended. The treatment is expectant or hormonal or surgical, of which more anon.

This classification into three groups is an oversimplification (good for the great majority of cases, and helpful for teaching students what to look for), but there is a fourth group—the unclassified. In this the testis lies reasonably in the line of descent and may be called "high emergent", but can be pushed in all directions around the external inguinal ring and often appears to go into the neck of the scrotum. (I think sometimes in manipulation we draw the scrotal skin up over the testis and deceive ourselves.) These patients I have deferred and examined on repeated occasions. I think the majority of them conclude by being classified as having ectopic testes, and by being operated on.

Operation.

So we come to this position. First a clear diagnosis must be made, and we then say: in the retractile type, do not operate; in the ectopic type, always operate; in the true undescended type, operate only when one is sure that the testes will not be down by puberty.

That is sufficient background, I think, to answer the two questions why and when to operate on undescended testes.

The first question, why operate, is the easier to answer. Why operate on "true undescended testes" and "group 4"? There are at least six good reasons.

Firstly, recurrent attacks of pain are experienced. These pains may be due to minor traumata, mild recurrent torsion, or unnoticed hernia, and whatever the cause, will result in fibrosis of testis and atrophy.

The second reason is torsion—either an acute attack, in which case operation must be performed within a few hours, or the mild recurrent attacks of torsion already referred to.

The third is the presence of hernia, which is stated to be present in 70% of "undescended testes". This often precipitates surgery by being painful or becoming obstructed. In leaving a hernia untreated while waiting for the testis to be more favourable for surgery, one runs a risk of losing the testis.

The fourth reason is potential malignant disease, which in the imperfectly descended testis is 22 times more common than in the normal, but even so the actual occurrence is very infrequent. It has been shown statistically that orchidopexy has little effect on the possibility of subsequent malignant disease.

The fifth and most convincing reason for operating is that most retained testes are not capable of spermatogenesis.

The last reason is psychological stress. It has been argued that in unilateral undescended testes we are not concerned with sterility, but what self-respecting adult male would not rather have both testicles in the scrotum? Patients with genital abnormalities conceal them and are very reluctant to discuss their reactions to them. The acuteness of their psychological distress in being different from their fellows may therefore not be generally realized. It may even result in suicide.

Concerning when to operate, torsion, hernia and pain are indications that force the surgeon's hand, but the real surgical problem concerns operating to improve fertility. The crux of this problem is how long we can afford to leave the testis in an abnormal situation without fear of permanent damage. I do not think that question has yet been scientifically answered. Every year of age from three to seventeen has its advocates as the best time for an elective operation.

If one decides to operate when the patient has reached puberty, one soon finds that one cannot fix any particular age for operating. I have found a familial tendency in some families—often the slender tall types—for puberty to be very late and the boy to be undersized and immature and then suddenly to shoot up at a great rate to six feet or more.

The "rule of 5" is useful in considering the stages of development of the normal testis. These stages are:

1. From origin to birth: The testes descend because of the high content of chorionic gonadotrophins in the maternal circulation.

2. From birth to five years: The testis is static and physiologically functionless because it is not receiving any gonadotrophic stimulation.

3. From five to ten years: The testis is growing very slowly and remains tiny.

4. From ten to fifteen years: Maturation is proceeding for reasons which are quite unknown. The anterior lobe of the pituitary begins to secrete effective amounts of gonadotrophic hormone which stimulates the gonads. Under this influence, the interstitial cells of Leydig secrete testosterone, and at the same time the hitherto inert germinal epithelium of the seminiferous tubules begins to proliferate and to differentiate into spermatozoa. The growth of the testis at this stage is very rapid.

5. From fifteen years onwards: Maturity is developing.

Having seen too many patients operated on by those without sufficient knowledge or technique, so that some months after operation, examination revealed either nothing in the scrotum or else a nodule not much bigger than a pea, and having seen too many orchidectomies performed because of the technical impossibility of bringing down a testis with a short cord, I held the opinion twelve months ago that the longer one deferred operation the better, until the first signs of puberty were approaching. Quite a case could be made out for delay—it would be better to sacrifice all chance for a testicle which might not be much good anyhow, by operating too late, than to injure a good testicle that was slow in

descending, by operating on it. Testicular biopsies performed at that time made it seem that, contrary to general opinion, all testes looked alike histologically before puberty, whether the patients were very young or older, whether the testes were ectopic or normal in position. Puberty seemed to be the latest safe period for operating successfully. Animal experiments showed that normal testicles put into a new environment, or prevented from descending, lost their powers of spermatogenesis, but regained them when the testicles were replaced in the scrotum.

If operation was performed too early, the blood vessels would be frail and tiny, and the chance of damage and subsequent atrophy greater than later; they would also be very short, and efforts to lengthen the vessels by retroperitoneal dissection, in spite of the greatest care and experience in handling these delicate structures, would be liable to cause a certain amount of injury.

The "intrasaccular" type with short cord and vessels prolapsed into a hernial sac requires a knowledge of all the surgical tricks for successful operation. However, in view of recent work, I think earlier operation should be performed, particularly on definitely ectopic testes.

There is evidence, put forward last year by Robinson and Engle, that unless the testis is placed in the scrotum before the patient is five years of age its spermatogenic function will be permanently injured. They make four points:

1. Up to five years the undescended testis is indistinguishable from normal.

2. It then shows retardation in the development of the spermatogenic elements, the tubules and cells appearing smaller in actual size, and the interstitial tissue being increased. These histological changes are confirmed by our own testicular biopsies.

3. It grows during puberty, but rarely becomes normal.

4. After orchidopexy performed before puberty, only a proportion of testes develop normally.

The explanation of this last fact may be as W. O. Nelson has suggested: (i) Some testicles are constitutionally defective; this results in faulty development leading to an ectopic or undescended position, but it also shows a paucity of germinal cells. (ii) Others are intrinsically normal, but fail to descend because of (*a*) inadequate hormonal stimulation, (*b*) some mechanical obstruction.

To sum up, I would say: let the surgeon see the patient when he is six to seven years old at the latest.

If the surgeon decides that the testis is ectopic, he will operate at once. If it is a unilateral true undescended testis, he will probably wait to see whether it will come down spontaneously.

The administration of a course of 10 injections of 500 units of "Antuitrin S" twice weekly would be the counsel of perfection. Animal experiments and clinical observations have shown that this causes the testicle to increase in size, and the vessels and spermatic cord to lengthen. It is also difficult to assess accurately the results of hormone therapy and to be sure that cures attributed to injections would not have occurred spontaneously when the patient produced his own hormones in sufficient quantities.

From a practical point of view I often dispense with this preliminary course. Considerable local discomfort and mental strain are associated with repeated injections. The injections are expensive, and bitter disappointment follows when it is announced that they have not been successful and that an operation will be necessary.

Hormones are therefore reserved for those patients with signs of endocrine imbalance and with bilateral undescended testes. Unilateral testes which are grossly small should be removed. Bilateral undescended testes when descent has not occurred after the administration of hormones are a "surgical headache". As soon as practicable, one side should be explored and the testis brought down, if necessary in two stages. If this is successful, the other side can then be tackled.

In all cases of undescended testicle I would strongly advocate that the surgeon who may eventually operate should take charge of the management of the case from the beginning, so that he can determine from repeated observations when is the optimum time to operate if that is necessary.

CHILDHOOD SCHIZOPHRENIA.[1]

By JOHN F. WILLIAMS,
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ADULT schizophrenia is of course well known, and is in fact the cause of more invalidity requiring hospital care than any other disease. Childhood schizophrenia is, however, less well known.

It was the late Dr. Albert Phillips who, in the years immediately preceding the recent war, first aroused my interest in this problem by asking if I had noticed an apparently increasing number of rather odd children, whose parents gave a history of the child's apparently normal development in infancy with a marked lack of development in the early years of childhood.

The war years did nothing to maintain my interest, but since then there seems to be a rapidly increasing number of such children characterized by oddities of development and behaviour and in particular by a marked aloofness from emotional contact with human beings. The same phenomena have been noted overseas, and it seems either that awareness of the problem has led to increased recognition or that such cases are in fact on the increase.

The term "schizophrenia" has not been approved by all authorities, and "atypical" and "autistic" have also been rather widely used. Adolph Meyer defined schizophrenia as "an abnormal reaction which certain individuals develop as an inadequate adaptation to the total life situation", and Potter states that "in children the symptomatology is found in the field of behaviour and a consistent lack of emotional rapport".

In children, differentiation in types is less definite even than in adults, but three broad classes are recognized according to the mode of onset.

The first class has an acute onset with previous apparently good behaviour and *rapport*, sometimes very good because of submissive and obsessive perfectionism. Then after illness or psychic trauma, operation or bereavement *et cetera*, the child drifts out of touch with people in its environment and shows anxiety, disorders of sleep, restlessness and speech disorder, perplexity, occasional hallucinations and odd bodily sensations. Recovery after a few days or weeks may occur, but sometimes there is no recovery, or recovery occurs with defect, or there may be temporary remissions only. No clear evidence of encephalitis or meningitis is to be obtained in these cases.

The second class is characterized by an insidious onset, with gradual withdrawal from affective contact with people, loss of interest in play, a tendency to brood on matters of personal concern, and preoccupation with abstract concepts, dates, measurements and names. Aggressiveness and destructiveness may often be present. There may also be hoarding of rubbish and repetitiveness in activity. Sometimes loss of speech occurs.

The third class is one of infantile autism with withdrawal characteristics within the first twelve months. These children are often thought to be feeble-minded or deaf because speech is late in development. They show fundamental inability to relate in a normal way to people. They give an impression of being self sufficient, of "silent wisdom", and are reported to be "not cuddlesome" from birth. There is difficulty in speaking. Names and parrot-like repetitions may occur, but the child often speaks of himself in the third person up to seven years, and speech

[1] Read at the annual meeting of the Australian Paediatric Association, Canberra, April 21 to 24, 1955.

shows lack of flexibility and is useless for communication. There is a pronounced desire for sameness in his surroundings. The child shows some interest in objects and often in complicated block designs, and may play for hours in a repetitive way with a piece of string. Pleasure is shown in the control of these and his own body, but people are just objects and conversation means little if anything.

The characteristics of all three groups appear to be withdrawal from emotional contacts with odd behaviour and development, and Dr. Gavin Flanagan has suggested that this withdrawal may be compared to the amœba which withdraws its pseudopodia in an unfavourable environment.

Ætiology.

"No specific cause of a specific disease called schizophrenia." We have to consider the child, his environment and the relationship between them. Kanner emphasizes the relationship of parental attitudes and human agents as an explanation of the symptoms, and states that this is possibly the reason why the children withdraw. However, parents will often complain that children are different from the start—not cuddlesome like the others, even though they cling like limpets. The parents are often intelligent, obsessive and lacking in warmth, aggressive, over-solicitous, over-anxious and rejecting. The grandparents are quite often notabilities.

Bender thinks that the cause is a diffuse encephalopathy with disorders of function at all levels, vegetative, intellectual, emotional, social or motor, but with varying incidence depending on previous personality make-up. There may be anxiety, due to disrupting effects of the disease, or to the sense of deprivation. This may be associated with a panic state, bewilderment or apathy. Inability to make emotional contacts with other people is a prominent feature. The vaso-vegetative functioning is disturbed in various ways, for example abnormal growth, precocious or delayed puberty, loss of rhythmic activities such as sleeping, eating or toilet function. Flushing and pallor or sweating may occur. Motor functioning is often clumsy or awkward, with anxiety in development of new bodily habits, sometimes with excessive bodily dependence on the mother. There is retention of early reflex activities, for example, whirling, bodily dependence and cohesiveness with preoccupation with, and repetitiveness in, bodily activities. The perception of the world seems strange and peculiar with unusual relationships, and there is excessive concern with abstract problems, for example life and death, but also with intellectual exercises, such as measurement and counting. Disturbance of body image in speeech and drawing and painting is often present. Mutism may occur as a result of regression or it may be the initial complaint. Speech is often unintelligible. Socially the child may be attractive and appealing by reason of his oddity, but there appears to be no true emotional response. Test results are markedly uneven with unpredictable breaks. The evidence for encephalopathy is rather inconclusive, but so are some of the figures for disturbed parent-child relationship.

The prominent feature is withdrawal of interest in persons, and this may be not only a symptom but possibly the cause, but why? And why does it occur at times so very early and from what? There may be total avoidance or avoidance only of speech, of looking or of hearing and not of bodily contact, which serves to emphasize the child's own individuality and identity as opposed to distance senses which emphasize outside objects.

One recent attempt at explanation by Rabinovitch and Dubo has been that there is a fundamental inability to experience a clear-cut consciousness of self and of the identities in the environment, that is, an amorphousness of perceptual experiences with a lack of distinction between self and surroundings. This may perhaps fit in with Bender's hypothesis of an encephalopathy and disturbance of the body image, but it is not so apparent as the affective disturbance and lack of affective response and selective withdrawal of interest which seems fundamental.

Some intellectual retardation may be present, possibly from the start, but this does not seem to be a primary factor in causation. There may also be physiological factors —for example, low energy level and a poor cardio-vascular system. Effects of minimal cerebral damage due to birth injury, or some enzyme defect or aberration of amino acid metabolism leading to lack of maturation or disorder of perception are also possible factors in some cases. A similar picture can occur with gross cerebral damage or with sensory deprivation—for example, deafness or blindness.

It seems to me that many children have a special faculty for autistic withdrawal from a situation of emotional difficulty, and at times this is used as a temporary protection, just like a curtain dropping when unpleasant topics are touched upon, and the diagnosis of *petit mal* had been suggested in one patient. The child, when blank, is not unconscious, may be destructive or cruel, but is just "not there". This may be an exaggeration of shyness or embarrassment. In some this habit may persist and become built in as a permanent reaction when faced with difficult situations.

Lack of empathy or *rapport* with someone has a marked effect on development in every respect, particularly language, and hence the mutism. Work on the effects of institutional life in determining intellectual retardation is of considerable significance in this regard, though it would seem that something different from complete deprivation is present, for many of these children have clever and painstaking parents.

It is, however, found in all cases which I have seen that the early backgrounds have been grossly unsatisfactory in so far as there has been emotional coldness and deprivation of human love and sympathy. The one common factor in all these cases has been just this fault in the relationship between parents and child, but it is my belief that this mechanism of withdrawal from emotional contacts is the cause of childhood schizophrenia and not merely a symptom.

Withdrawal seems something different from psychoanalytic regression to early stages of development. It certainly seems that the child is not particularly interested in anal or urethral pleasures, though oral mannerisms are frequent. The most prominent interest appears to be in repetitive manipulations with, for example, bits of string, blocks, gramophone, turning taps or light on and off, or abstract or intellectual problems, or maintenance of existing material order. Possibly this serves as a protection from anxiety.

It appears at least possible that there may be varying grades of withdrawal, with in some cases resulting defects of adult personality—for example, the cold, affectionless, withdrawn schizoid type, but with no definite psychotic picture—while in others the withdrawal is definite and absolute, and the end result is one of complete disintegration of personality, with the need for institutional care for life.

Diagnosis.

Diagnosis should be suspected in every severely disturbed child; this applies particularly to those with speech disturbances, for example mutism or neologisms, regression, seclusiveness, withdrawal, preoccupation with trifles, oral mannerisms such as biting, sucking, grimacing, or excessive anxiety.

Prognosis.

Prognosis appears dependent on reestablishment of empathy and relationship with a play therapist and with parents if possible. Treatment is often prolonged—eighteen months to three years in severe cases if there is any chance of permanent change, and even then the child often seems to be odd. In minor cases with withdrawal and mutism the prognosis is better. Physical methods of treatment have proved rather disappointing.

Many of these children in the past have been regarded as mental defectives, and many have been regarded as deaf, and the differential diagnosis between these groups is at times still difficult.

The numbers of cases diagnosed are still not great, but are sufficient to make it incumbent on all pædiatricians

at least to be aware of the need for attention to this group of problem children.

It may well be, as Winnicott has said, that "prophylaxis against psychosis is therefore the province of the pædiatricians, did they but know it", and that in the investigation of these cases may be found the clue to the prevention and treatment of schizophrenia.

THE DIAGNOSIS OF HÆMORRHAGIC STATES IN CHILDHOOD.[1]

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DURING the past fifteen years an enormous amount of good research has been carried out on the problems of blood coagulation and recently as many as ten new papers on this subject have been published each week. Many fascinating discoveries have been made which can guide the physician towards an exact diagnosis and which may also help him with the prognosis and treatment. However, an inevitable, unfortunate result of the vastly increased knowledge available on this subject is that precision in diagnosis has been gained at the cost of simple comprehensibility. Numerous tests have been devised for measuring coagulation disorders, and to understand the subject today one needs to give it some special study. In fact, when the physician wonders where to start investigating a patient with a hæmorrhagic state he may sometimes feel like A. A. Milne's character:

> There was once an old sailor my grandfather knew
> Who had so many things which he wanted to do
> That, whenever he thought it was time to begin,
> He couldn't because of the state he was in.

So, when eighteen months ago the Royal Children's Hospital granted the funds for research in hæmatology, priority was given to the problem of determining which tests were of the greatest practical value in the diagnosis of hæmorrhagic states in children.

Mechanism of Blood Coagulation.

Before I discuss the problems of diagnosis it will be helpful to consider the mechanism of blood coagulation. When the classical theory was propounded by Morawitz in 1905 (Figure I) it was known that the insoluble end-product, fibrin, was formed from a soluble precursor, fibrinogen, through the enzyme-like action of thrombin. It was correctly postulated that thrombin, which is normally absent from the circulating blood, was formed from a precursor, now called prothrombin. Calcium was known to be essential in the early stages, but there was uncertainty as to the nature and source of the factor which initiates clotting *in vivo*. Morawitz believed that the platelets were responsible for this factor and that it was an enzyme, thrombokinase (thromboplastin), and later workers substantially confirmed his views. It is a great tribute to Morawitz that after fifty years his classical theory has proved so well founded, it forms the basis of all the investigation techniques now in use. Today it seems that, as Macfarlane puts it, to become a maker of theories is the final stage in the evolution of the individual coagulation worker: there is thus a further tribute to Morawitz in the fact that when he formulated his theory he was only twenty-six years of age.

Some expansion of the classical theory has since been made necessary by the results of intensive research on the mechanism of coagulation with the discovery of new coagulation factors. Three modifications of the classical theory are of importance to clinicians. In the first place, as was postulated by Nolf, two decades earlier, the rapid conversion of prothrombin to thrombin has been shown to require factors in addition to thromboplastin and calcium (Figure II). In the latter half of the second World War Owren in Norway, Quick in the United States of America, and Fantl and Nance in Melbourne independently reported the discovery of factor V, labile factor or prothrombin accelerator. This factor, like prothrombin, is a normal plasma constituent. Deficiency of it leads to a hæmorrhagic state clinically resembling hæmophilia in many respects and called parahæmophilia. Another factor needed for the conversion of prothrombin is factor VII, convertin or serum prothrombin conversion accelerator, which is present in serum as well as in plasma. The existence of this factor was suspected by Owren and by others for several years before Alexander *et alii* in 1951 discovered patients who were bleeding through lack of it. Deficiency of either

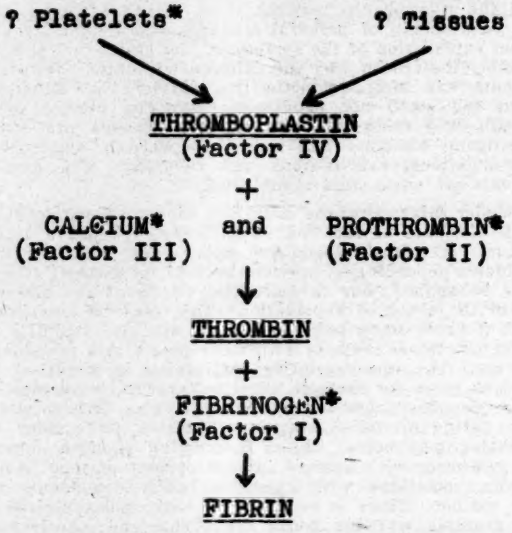

FIGURE I.
Classical theory of coagulation (Morawitz, 1905).
* = present normally in blood.

of these prothrombin conversion or accelerator factors may be congenital and familial, or it may be acquired, for example, in severe liver disease, and in the newborn infant factor V deficiency occurs as a transient physiological state coincident with the hypoprothrombinæmia. Fortunately these two deficiencies are uncommon except in the neonatal period, but there is an important point that the physician must bear in mind, namely, that with such deficiencies the plasma prothrombin level appears low as estimated by Quick's one-stage test, even though it is really normal.

The second important expansion of the classical theory concerns the formation of thromboplastin. This enzyme-like factor is not derived directly from the platelets. It is formed when a lipoid factor released from platelets reacts with plasma precursor substances or prothromboplastins in the presence of calcium and, apparently, factor V and factor VII. Tissue injury, on the other hand, yields directly this end-product, thromboplastin. These thromboplastin precursors have received an enormous amount of study and publicity in the last three to five years. Hæmophilia for two decades has been recognized as due to congenital deficiency of antihæmophilic factor or antihæmophilic globulin, and now this substance is considered to be a specific thromboplastin precursor, referred to by Fantl and Sawers (1954) as α-prothromboplastin, and often simply called AHF. Likewise, the so-called Christmas disease, which clinically is almost identical with AHF deficiency, is due to lack of another specific thromboplastin precursor which Fantl and Sawers call β-prothromboplastin; others have given it such names as plasma

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

thromboplastin component (PTC), plasma factor X, Christmas factor, and antihæmophilic B factor. In the last eighteen months two more examples have been described of reputedly specific thromboplastin components or prothromboplastin (Rosenthal *et alii*, 1953; Spaet *et alii*, 1954), deficiency of which causes a syndrome resembling hæmophilia in many respects. Their names alone (plasma thromboplastin antecedent, and plasma thromboplastin factor –D) suffice to indicate the confusion that flourishes around this subject. For the ordinary physician, however, it is enough to remember that all these prothromboplastin deficiencies are identical with hæmophilia in their reactions to the old-fashioned routine coagulation tests, and that their differentiation—which really is worth while—requires the facilities and the experienced workers of a modern

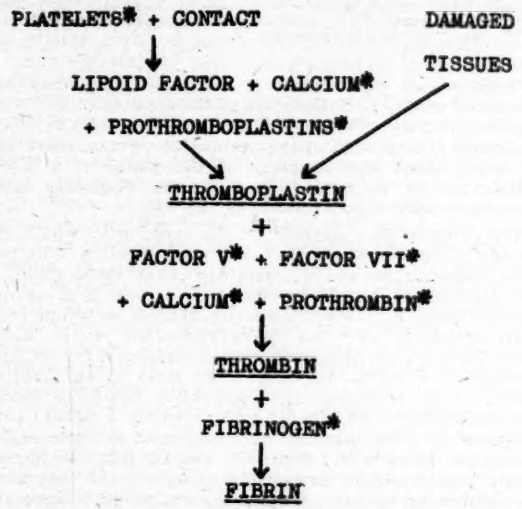

FIGURE II.

A modern theory of coagulation, excluding inhibitors.
* = present normally in blood.

hæmatological laboratory. The only other important modification to be made in the classical theory is to incorporate the concept of coagulation as a dynamic process in which positive or coagulant forces are competing more and more successfully against negative, inhibitor or anticoagulant forces, with chain reactions producing increasing acceleration of thrombin formation, until with an almost explosive climax this reaches the critical level necessary for the formation of the gelatinous clot. The latest theory of coagulation, published by Owren (1954) only four months ago, in addition to showing the complexity and terminological confusion of modern theories, does also give an indication of the dynamic nature of coagulation and of the autocatalytic action of thrombin, which, once slowly formed, accelerates the activity of factor V, and according to some workers also accelerates the disintegration of platelets.

Clinical Diagnosis.

Turning now to the diagnosis of hæmorrhagic states, as every physician knows, the history and clinical examination are valuable in screening the types of hæmorrhagic disorder, and they are usually indispensable for a complete diagnosis. Macfarlane considers that even in hæmophilia the clinical is fully as important as the laboratory diagnosis. The family history, to start with, may give an essential clue: in a majority of the hæmorrhagic disorders hereditary factors play some part (Table II) and the sex-linked pattern of inheritance is almost pathognomonic of α- and β-prothromboplastin deficiencies. Clinically it is important to look for evidence of trauma, of portal hypertension, and of a host of general disorders, such as infections, toxæmias, allergies, malnutrition, leuchæmia and reticuloses. In these days, when the spotlight is naturally falling on laboratory studies, it is worth reminding oneself of the vascular (as distinct from the hæmic) causes of bleeding, and amongst these hypertension is a factor easily overlooked in children. One girl, aged eleven years, almost symptomless apart from epistaxes, was subjected to extensive hæmatological investigations and repeated blood transfusions before a careful clinical examination disclosed a blood pressure of 180 millimetres of mercury, systolic, and 120 millimetres, diastolic, due to unsuspected chronic nephritis with uræmia.

The nature and distribution of the hæmorrhagic lesions often provide a simple yet valuable clue to the diagnosis (Table I). Petechiæ occur when damage to the capillary

TABLE I.

Diagnostic Significance of Hæmorrhagic Lesions.

Lesion.	Significance.
Petechiæ	In capillary damage (toxic, infective, anoxic, allergic, scorbutic). In thrombocytopenic states, especially with less than 50,000 platelets per cubic millimetre.
Hæmorrhagic papules, vesicles.	In "allergic purpura", with characteristic distribution.
Ecchymoses ..	In all hæmorrhagic disorders.
Hæmatomata ..	In hypoprothrombinæmia, hæmophilias and severe purpuras.
Hæmarthroses ..	In hæmophilias; rarely in parahæmophilia and other hæmorrhagic disorders.
Internal hæmorrhages, epistaxes.	In all hæmorrhagic disorders.

endothelium has been caused by, for example, toxic, infective, allergic, anoxic and scorbutic states, and when the platelet count is reduced below 50,000 per cubic millimetre. They are not found typically in the hæmophilic disorders nor usually in deficiencies of the prothrombin complex. Hæmarthroses on the other hand are almost confined to the hæmophilias or prothromboplastin deficiencies and seldom occur in the parahæmophilias and other hæmorrhagic disorders. Their differentiation from the joint effusions of Schönlein's purpura is usually simple, but the paraarticular hæmorrhagic swellings of scurvy and leuchæmia may provide diagnostic problems. When in doubt, X-ray examination of the hæmophilic joint sometimes reveals characteristic rounded decalcified patches due to hæmorrhages. Hæmatomata are most likely to be due to prothrombin deficiency or to one of the hæmophilic disorders, and they occur in purpuras only when the condition is severe. Œdematous nodular or papular lesions, often associated with various forms of hives, are seen only in so-called allergic purpura. In this condition the distribution also is diagnostic, the lesions being maximal where venous congestion is greatest, which is usually on the legs and buttocks. The distribution can also be diagnostic in other cases. A country girl of twelve years was twice sent to hospital with recurring purpura, investigation of which was fruitless. The peculiar limitation of the lesions to the anterior aspects of the upper arms led to the correct diagnosis of anxiety hysteria with self-inflicted ecchymoses from biting.

In many hæmorrhagic states the capillary fragility test or tourniquet test of Hess is a handy clinical tool, if properly used. When the patient's blood pressure is taken, the sphygmomanometer cuff is applied just above the cubital crease, and the width of a penny below the cuff a circle the size of a penny is outlined on the skin with a ball-point pen. Any lesions already present within this circle are marked with the pen. The blood pressure is then taken, after which the cuff is kept inflated for five minutes at a point midway between the systolic and diastolic pressures. When the pressure is released it is wise to wait a further five minutes before counting the number of petechiæ visible in a good light inside the penny circle. The child in perfect health will have less than eight petechiæ present, while in severe purpura there may be 200 or more. This test gives a measure of the perme-

TABLE II.

Diagnostic Characteristics of Hæmorrhagic States.

Disorder.	Hereditary.	Type of Lesion.	C.F.T.[1] Result.	B.T. Increased.	Platelets Decreased.	C.R. Poor.	C.T. Increased.	Fibrinogen Decreased.	Prothrombin.	
									Concentration Decreased.	Consumption Decreased.
Allergic purpura	±	O., P., E., I., J.	+	−	−	−	−	−	−	−
Symptomatic purpura	−	P., E., I.	+	±	±	−	−	−	−	−
Idiopathic thrombocytopenia	±	P., E., I.	+	+	+	±	−	−	−	+
Hereditary thrombasthenia	+	P., E., I.	±	+	−	±	−	−	−	±
Hæmophilias	+	E., H., I., J.	−	−	−	Late	+	−	−	+
Parahæmophilia	±	E., H., I.±J.	−	−	−	−	+	−	+	+
Hypoprothrombinæmia	−	E., H., I.	−	−	−	−	±	−	+	−
Fibrinogenopenia	±	E., I.	−	−	−	+	+	+	+	−

[1] "O." = œdematous, nodular lesions; "P." = petechiæ; "E." = ecchymoses; "H." = hæmatomata; "I." = internal bleeding; "J."=hæmarthroses; "C.F.T." = capillary fragility test; "B.T." = bleeding time; "C.R." = clot retraction; "C.T." = clotting time; prothrombin concentration and consumption refer to results of Quick's one-stage methods; "+" = yes; "−" = no; "±" = may or may not be.

ability of the capillaries to red blood cells. The capillary fragility or permeability will be increased if there are insufficient platelets to plug the normal interstices, as in severe thrombocytopenias; and if the capillaries are lacking in intercellular cement, as in scurvy; and if the capillary endothelial cells are damaged or distorted by, for example, infections, chemical toxins, allergic reactions, cachectic states *et cetera*, and in hereditary thrombasthenia; and vascular damage also may be the major factor in producing an increased fragility in the immunovascular form of thrombocytopenic purpura. The test is useful in diagnosis because in hæmorrhagic states other than the groups just mentioned it gives normal results. A practical point, however, is that a positive result may revert rapidly to a normal one, as may be seen, for example, in a case of scurvy or of allergic purpura after a day or so of treatment. A normal result therefore does not exclude the conditions mentioned above if the test is done after the height of the illness.

As the foregoing statements indicate, in many cases the clinical evidence will allow the diagnosis to be made with a reasonable degree of certainty and in others it enables the physician to go a long way towards placing the hæmorrhagic state in the appropriate category, thus speeding up the procedure of laboratory investigation.

Laboratory Diagnosis.

It is unnecessary to emphasize the importance of the full blood count and stained films, which may give evidence of thrombocytopenia, of leuchæmia, of infections, of allergy and of causes of anæmia other than hæmorrhage. Estimation of the bleeding time by Duke's method measures chiefly the ability of injured capillaries to contract; its relation to the adequacy of the platelets is a remote one. It is prolonged in the presence of damaged or distorted capillaries and in the more severe states of thrombocytopenia, and occasionally, too, when there is deficiency of a very gross degree of prothrombin and other coagulation factors. A normal result is of limited value in excluding disorders of the capillaries and of the platelets. It must be recognized that technical errors tend to shorten the bleeding time, not to lengthen it. Measurement of the rate and degree of clot retraction provides information about the adequacy of the platelets and of fibrinogen; and as fibrinogen is rarely deficient, poor clot retraction usually implies numerical or functional deficiency of the platelets (Table II). When the platelets number less than 70,000 per cubic millimetre, clot retraction is usually impaired; so its measurement provides a rough check on the platelet count, in addition to being of some assistance in the rare conditions of hereditary thrombasthenia and fibrinopenia. Investigation of clot retraction, however, is less often of use in diagnosis than determination of the capillary fragility and the bleeding time. These last two tests are done routinely, not only because they are very simple to carry out, but because they may give information of great value, provided it is recognized that they are concerned chiefly with the state of the capillaries, not with platelet activity. Whenever the tests so far described, including examination of the stained blood film, leave one in doubt about the adequacy of the platelets, a direct platelet count is needed, and precise diagnosis often requires a marrow puncture biopsy as well.

The clotting time depends on the speed with which the various phases of coagulation take place *in vitro*. The test aims at measuring the coagulability of the blood alone, in the absence of tissue factors, but it has been shown recently that it is extraordinarily difficult to avoid technical errors in this test. Contamination of the blood specimen with the thromboplastin in traces of tissue juice artificially shortens the coagulation time to an amazing degree. So sensitive is hæmophilic blood to added thromboplastin that in a case with a clotting time increased to forty minutes the addition of as little as 2% of normal blood will restore the clotting time to normal levels, and Fantl and Sawers (1955) have found that when the aspirating syringe and needle are pointed down the arm the clotting time is 40% longer than when they are directed up the arm. The capillary tube method of Wright is particularly prone to give misleading results, which may be too low from admixed tissue juices or too high if the test is performed in cold weather. Thus even if the temperature is controlled, the resultant clotting time is of diagnostic significance only if it is prolonged. If a hæmorrhagic state is clearly present, the more reliable test-tube method of Lee and White should be used, despite the practical difficulties sometimes involved with small children. This method may be made more sensitive by using silicone-coated syringe and test-tubes. Silicone lengthens the time of clotting by delaying the formation of coagulant substances (which is accelerated by contact with glass), thus allowing minor defects of coagulation to be detected. Deficiency of any of the coagulation factors in the patient's blood may prolong its clotting time. Assay studies of coagulation factors in deficient individuals indicate that the concentration of a coagulation factor in the patient's blood may fall to a quarter of the normal level before there is any prolongation of the clotting time. Thus blood with as little as 30% to 40% of prothrombin will clot normally, and the same is generally true of AHF, of factor V, of fibrinogen and possibly of the other factors. Clinically, however, this is of little consequence because a similar reduction in the level of a coagulation factor in the blood may be present before hæmorrhage occurs. For practical purposes the Lee and White clotting time remains one of the most useful aids to diagnosis provided the test is properly and carefully performed.

It can be seen from Table II that the clinical data and the results of the tests described to date are sufficient for the diagnosis of the bulk of the purpuras, which are the commonest hæmorrhagic disorders of childhood. For the recognition and differentiation of the remaining groups,

more advanced laboratory procedures are essential. Here we enter the large and growing maze of modern hæmatological techniques, which some regard as ludicrously bewildering, but of which the physician today must have at least a smattering. Figure II may serve to illustrate the descriptions which follow.

The path leads first to the prothrombin complex. In a modification of the one-stage prothrombin test introduced in 1935 by Quick, the patient's plasma is mixed with optimal amounts of thromboplastin and calcium. The speed with which clotting occurs is generally related to the concentration of prothrombin present. By comparing this clotting time with that of a normal control, the estimated concentration of prothrombin in the patient's plasma can be expressed as a percentage of normal; in health the result lies between 60% and 140%. Unfortunately this test is not a specific measure of prothrombin, as Quick originally believed. When it is performed with a relatively pure, reliable source of thromboplastin, such as brain extract, the result of the test is influenced not only by the concentration of prothrombin in the plasma but also by the concentration of factor V, of factor VII, and of fibrinogen. Misleading low results may therefore occasionally be obtained from reduction of the concentration of any of these three factors or from the presence of excess antithrombins. In a child, aged eleven years, with hæmorrhagic symptoms for seven years, an estimated plasma prothrombin level of only 10% was found to be due not to prothrombin deficiency but to complete afibrinogenæmia. Reevaluation of Quick's one-stage test has thus become necessary, but it has not detracted greatly from its value as a practical guide to diagnosis. If the estimated plasma prothrombin concentration is low, additional tests are necessary to exclude the other possibilities just mentioned in order to establish that the patient has hypoprothrombinæmia. If the result is normal, attention is next directed to the thromboplastin group of factors.

When normal blood or plasma clots, most of the prothrombin is used up and very little of it can be found in the serum. By estimating the concentration of prothrombin in plasma before clotting and the concentration in the serum after clotting, a measure is obtained of the amount of prothrombin consumed during the clotting process, and this is the principle of Quick's prothrombin consumption test. The amount of prothrombin converted to thrombin or "consumed" depends not on the concentration of prothrombin present before clotting but on the amount of thromboplastin that is available in the plasma to react with the prothrombin. Therefore patients unable to produce thromboplastin in normal amounts will show decreased consumption of prothrombin. This may arise when the platelets are inadequate in number or in quality, when prothromboplastins are deficient, as in the hæmophilias, when factor V or factor VII is deficient, and in the rare cases with excess of antithromboplastin inhibitors or anticoagulants. Quantitative deficiency of the platelets will have been already detected, and hereditary thrombasthenia with a qualitative platelet defect may be indicated by the family history, bleeding time, clot retraction and normal platelet count.

To differentiate the remaining disorders with thromboplastin deficiency, recalcified clotting times of mixed plasma samples are employed. Plasma samples are obtained from other patients known to be deficient in certain factors, for example, a hæmophiliac with deficiency of AHF or α-prothromboplastin, or a patient with so-called Christmas disease with deficiency of Christmas factor or β-prothromboplastin. Use is also made of samples of normal plasma artificially rendered deficient in certain factors by adsorption with barium sulphate or aluminium hydroxide (which remove Christmas factor and factor VII but not AHF or factor V). To perform this test, calcium chloride is added to the patient's oxalated or citrated plasma, and the time taken for the plasma to clot is measured accurately. In any patient with a deficiency of thromboplastin this recalcified clotting time will be prolonged, but it can be restored or corrected to normal by the addition of any plasma known to contain the factor which the patient's plasma lacks. (A rare exception is the patient with hæmorrhage due to a circulating anticoagulant, which requires investigation by other methods.) Then to a series of tubes containing the patient's plasma are added various samples of plasma and serum, each known to be deficient in one factor, and the effect produced by these additions on the recalcified clotting times of the mixtures indicates which factor is lacking in the patient's plasma.

Excellent though these recalcified clotting time tests are in most respects, they do require adequate stocks of plasma and serum known to be deficient in certain factors. Because these are not always readily accessible, an alternative and in some ways a better procedure has been found to be the thromboplastin generation test of Biggs and Douglas. This test makes use of a system containing washed platelets, plasma adsorbed with aluminium hydroxide, serum and calcium; this mixture is added to platelet-poor plasma and the clotting time noted. By this method the effects of various coagulation factors on the patient's ability to generate thromboplastin can be assayed separately, and so the factor missing from the patient's plasma can be deduced. The thromboplastin generation test is now performed as a routine investigation. It can be modified to give semi-quantitative results. In addition to the above, there are a number of other tests which can usefully be employed in selected cases. Examples of these are methods for assaying various coagulation factors to determine their concentration in the blood. A method for assaying AHF, for example, has a place in confirming the diagnosis of hæmophilia in doubtful cases, being used to corroborate the results obtained from recalcified clotting times and from thromboplastin generation tests.

Conclusion.

It is no longer possible in these times to make the diagnosis of hæmorrhagic disorders appear simple. The aim in this paper has been to show only that the problem can be tackled in an orderly fashion, that it must commence at the clinical level, and that highly skilled technical assistance in the laboratory is often essential. The modern laboratory has demonstrated how helplessly the clinician was floundering in a sea of ignorance when the film, the bleeding time and the clotting time were the sole flimsy flotsam at which he could clutch for diagnostic support, and how buoyant he can now feel with the shining light and life-line of science about him. The way is open for clinicians to grasp that life-line firmly with both hands and make full use of all its diagnostic threads, and thus avoid the reproach earned by A. A. Milne's nautical no-hoper, the shipwrecked sailor who

> . . . never could think which he ought to do first.
>
> So in the end he did nothing at all,
> But basked on the shingle wrapped up in a shawl.
> And I think it was dreadful the way he behaved—
> He did nothing but basking until he was saved.

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INFECTIOUS LYMPHOCYTOSIS.[1]

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THE purpose of this paper is to describe the occurrence in a small group of children, patients in the Royal Children's Hospital Orthopædic Section at Frankston, of a condition which had the features described in infectious lymphocytosis. It seemed at one time that several children might have this condition, but eventually only three were accepted as fulfilling the necessary criteria. Nevertheless, in spite of the small number this occurrence has its clinical value, and so far as I know, true examples of infectious lymphocytosis have not previously been described in Australia. Moreover, interesting conjectures arise from the development of pertussis in the hospital a few weeks later.

Discovery of Lymphocytosis.

The story opens with the chance discovery in the course of routine blood examination of a high degree of leucocytosis, with predominating lymphocytosis, in two small children, sister and brother, aged two years and three and a half years respectively, who were receiving treatment for primary pulmonary tuberculosis, with segmental pulmonary collapse. Both had an original miliary infection and both had been in the hospital for the previous ten months. In the younger child (Catherine) the count was 112,000 per cubic millimetre, with only 6% neutrophile cells; and in her brother (James) the count was 85,600, with 12% neutrophile cells.

Six weeks after this discovery, a third small boy (Philip), aged three years, was found on purely routine blood examination to have a leucocyte count of 58,000, with 12% neutrophile cells. This boy was also receiving treatment for tuberculosis, but seemed very well indeed. These three children will be referred to as group A.

Previous Clinical History.

Although at the time of the finding of the lymphocytosis all three children appeared to be very well, a survey of the history showed that each had had a preceding rise in rectal temperature, to a maximum of 103° F. In two of the children (Catherine and James) the pyrexia had occurred twelve days before the lymphocytosis was found (Figure I), while in the case of Philip the fever occurred four weeks earlier. In none of them had obvious symptoms been present, but one child was noted to have inflamed tonsils.

Progress of Lymphocytosis in Group A Children.

In Case I (Catherine) the leucocyte count fell from 112,000 to 22,000 per cubic millimetre within ten days, with increase in the neutrophile cells to 22%.

In Case II (James) the leucocyte count fell from 85,600 to 44,000 per cubic millimetre within three weeks and to 12,000 within five weeks, with increase in the neutrophile cells to 52%.

In Case III (Philip) the leucocyte count fell from 58,000 to 22,000 per cubic millimetre within fourteen days, with an increase in the neutrophile cells to 50%.

It will be seen that the fall in the number of leucocytes was fairly rapid and followed a definite pattern. This will be contrasted later with the pattern in pertussis and in childhood tuberculosis.

Investigation of Staff and Other Children in Ward.

Fortunately for the purpose of observation and comparison this is a small twelve-bed ward of young children, most of whom were receiving treatment for tuberculosis.

All the staff had normal blood findings.

A routine survey showed three other children to have consistently raised leucocyte counts, with maximum of 18,000 per cubic millimetre (28% neutrophile cells), 22,000 (18% neutrophile cells), and 17,000 (26% neutrophile cells) respectively. These figures approximate those we have found in children with active primary pulmonary tuberculosis. Moreover, this has been a sustained lymphocytosis, quite different in pattern from those in Group A (infectious lymphocytosis). I shall refer to these children as Group B.

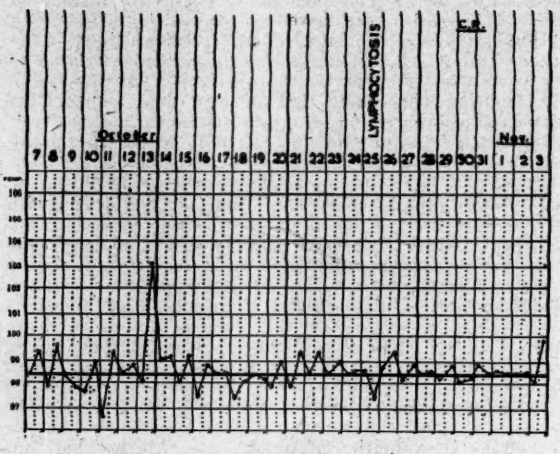

FIGURE I.

Occurrence of Pertussis.

Then came a complicating and an interesting feature, the occurrence of definite clinical pertussis in a child aged three years in the same ward. This boy was also being treated for primary pulmonary tuberculosis, and his

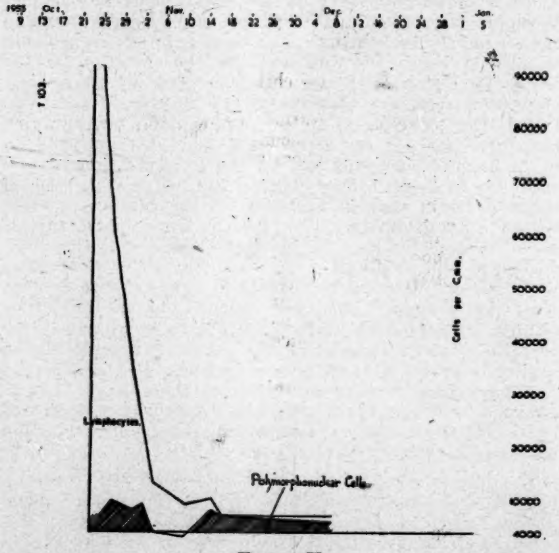

FIGURE II.

lymphocytosis was found approximately twelve days after the peak of the lymphocytosis in the third child in Group A. And finally, four weeks later, a group of six children in a different and geographically separate ward developed typical pertussis. These will be called Group C.

Investigations.

Group A (Infectious Lymphocytosis).

1. *Blood.*—The serum of these children gave the following results to tests in all cases: Paul-Bunnell, negative;

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 21 to 24, 1955.

influenza A, negative; influenza B, negative; mumps, negative; *herpes simplex*, negative.

2. *Pertussis Tests.*—Tests for hæmo-agglutination were carried out at the Commonwealth Serum Laboratories by Dr. Stephen Fisher, whose help I wish to acknowledge. Two patients gave positive results to a titre of 1:8, and it was later ascertained that both had received pertussis immunization eighteen months previously. In the third case the result was negative.

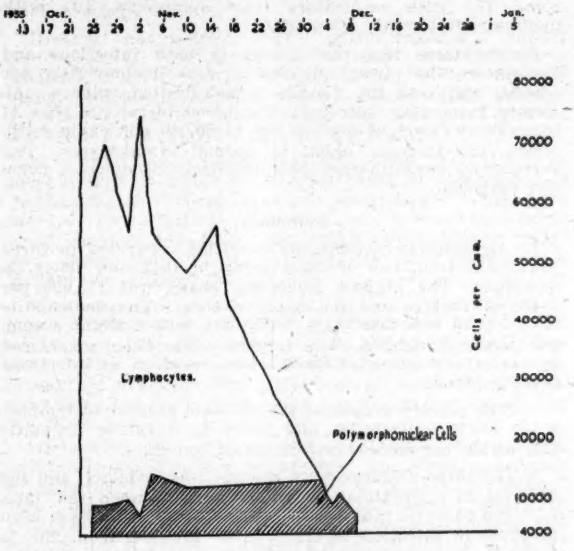

FIGURE III.

3. *Bone Marrow Biopsy.*—Bone marrow biopsy was carried out on only one child and did not reveal any definite abnormality, there being 42% lymphocytes and 1·6% lymphoblasts at a time when the peripheral blood showed a total leucocyte count of 22,500 per cubic millimetre, with 78% lymphocytes, 10% lymphoblasts and 3% monocytes. These estimations were carried out in the hæmatology department of the Royal Children's Hospital.

Group B (Doubtful Infectious Lymphocytosis—Probably Simple Tuberculous Infection).

Virus Investigation.—Within a day or two of the noting of the lymphocytosis, samples of blood, naso-pharyngeal secretion and fæces were submitted to the virus department of the Royal Children's Hospital. No virus has been isolated.

Group C (Clinical Pertussis).

Pertussis Tests.—Tests for hæmo-agglutination were performed on three of these children by Dr. Stephen Fisher at the Commonwealth Serum Laboratories. All results were positive, although in one instance the result was negative 46 days after cough commenced, but positive 100 days after cough commenced. The sera of several "controls" were submitted. In these cases the results were invariably negative.

Other Features.

Possible Incubation Period.

If the lymphocyte "peaks" of the three children in Group A are superimposed (Figure V), it is found that these are dated October 25, November 14 and December 8; this gives an interval of approximately twenty days between peaks. This could be evidence supporting an incubation period of approximately twenty days in "infectious lymphocytosis". Previous writers have estimated it to be between twelve and twenty-one days, whereas in pertussis it is probably between seven and fourteen days.

Pattern of Lymphocyte Count.

The pattern of the absolute lymphocyte counts in Group A children has been shown in Figures II, III and IV, and is of considerable interest. I am indebted to Dr. Loris Figgins for setting these out for me. In two of these children there is a dramatic fall within about ten days and in the third child within about twenty-one days.

The lymphocyte pattern in Group B children remains at a much more consistent level and is probably due simply to the healing tuberculous process.

The lymphocyte pattern in the children in hospital with clinical pertussis is broadly similar to that of Group B children. It consists of a long, gently sloping plateau (Figure VI) and corresponds very closely with that shown in Brennemann's text-book of pædiatrics (1950) for the weekly changes in the white cell count in 70 cases of pertussis.

Occurrence of Blast Cells.

The occurrence of blast cells is said to be uncommon in infectious lymphocytosis, but these were noted in two of the children in Group A. In one child the hæmatology department of the Royal Children's Hospital reported 10% blast cells in the peripheral blood. None was seen in the children with clinical pertussis.

Differential Diagnosis.

In my opinion the three children in Group A have been examples of infectious lymphocytosis. Other possible causes for the lymphocytosis will now be discussed.

Infectious Mononucleosis.

There was absence of (*a*) glandular and splenic enlargement; (*b*) the typical large, irregular and distinctive mononuclear cells in the blood picture; (*c*) the longer period of pyrexia; (*d*) the response to heterophile agglutination (Paul-Bunnell test).

Pertussis.

The fact that one child in the same ward and five children in another ward developed clinical pertussis is interesting. There is, too, the fact that in two of the three children in Group A the anti-hæmagglutinin titre

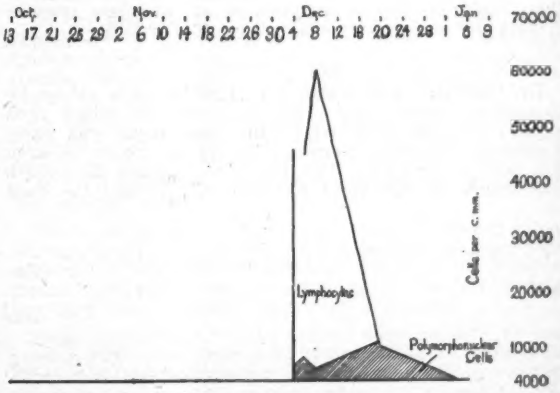

FIGURE IV.

was positive. However, they had both received anti-pertussis inoculation eighteen months previously, which could explain their positive result. This interpretation is supported by the fact that the agglutinin titre level in these two was 1 in 8 as against 1 in 16 for the children who had clinical pertussis.

The following facts are against a diagnosis of clinical pertussis. (1) These children were for many months under close ward observation by the same senior nursing staff without showing any clinical evidence whatever of per-

tussis. (ii) The leucocyte counts in these three Group A children—112,000, 85,600 and 58,000 per cubic millimetre—are very high indeed and much higher than is usual in pertussis. (It would be unusual for each of the three "grouped" cases of pertussis to have such a consistently high total. Dr. John Perry, in an unpublished investigation in 1951, found only one of 18 children with clinical pertussis to have a cell count as high as 40,000, the average being 21,000 per cubic millimetre.) (iii) The serial "pattern" of the lymphocyte level in the children regarded as having had infectious lymphocytosis is characterized in all three cases by the dramatic fall in the count within two or three weeks and has been entirely different from the pattern in pertussis, with its long, gently sloping plateau extending over many weeks.

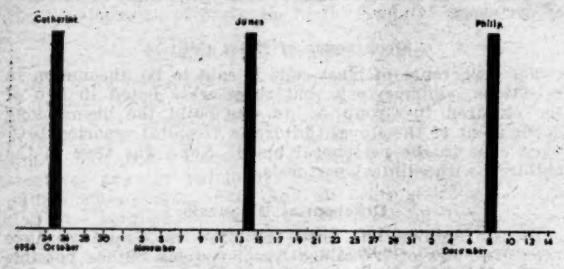

FIGURE V.

Tuberculosis.

All three Group A children were suffering from tuberculosis, with marked hilar gland enlargement. Undoubtedly tuberculosis does cause a degree of lymphocytosis, and Whitby and Britton (1953) quote Gardner and Mettier (1949), who found leuchemoid reaction of a lymphatic type in two adults who later died of miliary tuberculosis. However, a fairly large number of blood counts have been made by us on children with primary pulmonary tuberculosis, but without our finding a picture comparable to this I have described.

It is possible, of course, as Dr. John Colebatch suggested when he was good enough to investigate further one of these children, that a combination of infectious lymphocytosis and tuberculosis could cause this picture.

Drug Therapy.

Dr. Colebatch has drawn my attention to a report by Cannemayer and others (1955) on blood and lymph node studies in PAS sensitivity. In these there was early leuchæmic reaction. However, two of our three children had been receiving PAS for ten months before the sudden appearance of this blood picture. But perhaps the most

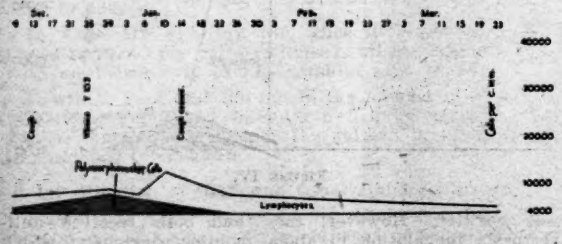

FIGURE VI.

important evidence against PAS therapy as a factor is that although PAS was discontinued immediately in the case of one child, no change in the blood picture occurred for approximately three weeks, while his sister's leucocyte count fell quite dramatically while she was still taking three drachms of PAS daily.

The Condition Designated Infectious Lymphocytosis.

Infectious lymphocytosis was first described as an entity by C. H. Smith, of New York (1941). It is not common, but several accounts are available and Smith gives a detailed account in "Advances in Pediatrics" (1947). He stresses the point that there are often few symptoms and that the condition is usually discovered on routine blood examination, and so most commonly in institutions.

Four groups are described (Scarletta *et alii*, 1954): (*a*) without symptoms, (*b*) with gastro-intestinal symptoms, (*c*) with respiratory tract symptoms, (*d*) with meningo-encephalitic symptoms.

Smith states that the disease is both infectious and contagious, that lymphadenopathy and splenomegaly are absent, and that the disease is self-limited, with a uniformly favourable outcome. The blood picture is that of hyperleucocytosis of over 40,000 to 50,000 per cubic millimetre, the increase being in normal lymphocytes. The heterophile agglutination test uniformly produces a negative response.

Summary.

1. An unusual lymphocytic condition occurring in three young children, two of them being brother and sister, is described. The highest leucocyte "peak" was 110,000 per cubic millimetre and the lowest 56,000. The neutrophile cells fell to less than 10% and there was a slight accompanying eosinophilia. The condition has been considered to have the features of the disease described as infectious lymphocytosis.

2. The pattern graphs of the absolute number of lymphocytes show uniformity, and there is a rather dramatic fall which commences within about ten days.

3. The three children were in close ward contact, and the interval of approximately twenty days between the "prefall" lymphocytic peaks suggests that there could have been progressive infection of these three children from one to another at an interval of approximately twenty days.

4. The later occurrence of pertussis in one child in the same ward and of six children in another ward complicates the picture, but makes it more interesting. Two of the three children with the picture of infectious lymphocytosis showed a positive result (1 in 8 titre) in the serum anti-hæmagglutinin test for *Hæmophilus pertussis*, but both had received anti-pertussis inoculation. The complete absence of cough and other features of pertussis in these children under close hospital observation makes it most improbable that they were suffering from clinical pertussis as we know it.

5. The suggestion is put forward, very tentatively and without sufficient statistical evidence, that there could be a relationship between infectious lymphocytosis and "subclinical" pertussis.

6. This study indicates the need for routine blood examination of children in long-stay hospitals. If this was combined with the carrying out of the serum hæmo-agglutination test for *H. pertussis* in all children showing an unusual degree of lymphocytosis, further light might be thrown on this subject.

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MEGAURETER.[1]

By F. DOUGLAS STEPHENS,
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THE problem of megaureter presents itself to the clinician either as a persistent or recurrent urinary tract infection, or as a cause of vague abdominal pain or hæmaturia. The enlarged ureters are found as a result of routine urinary system investigation, with special emphasis on micturition cysto-urethrography.

Urethral obstructions which cause secondary bladder and ureteral dilatation are excluded by the cysto-urethrography. Impacted urinary calculi, ureterocele, and spinal meningomyeloceles are associated with ureteral enlargement, but for these a ready explanation is available. All these are excluded from this discussion.

The following remarks deal only with that group of megaureters in which no obvious cause of obstruction is demonstrable. There are two subgroups. These are divided for practical purposes, by micturition cysto-urethrography, into those that permit vesico-ureteric reflux and those that do not—megaureter with reflux and megaureter without reflux.

The reflux group is commoner by 3:1. There were 23 cases in the series. Females predominated by 4:1, and the abnormality was bilateral in 22 out of 23 cases. The abnormality is presumably genetically determined. The presenting symptom was persistent or recurrent urinary tract infection in all cases—pain was absent and calculi did not form.

Micturition cysto-urethrography demonstrated free efflux and reflux of iodide into the ureters. The technique of this investigation consists of introduction of 16% "Uriodone" into the bladder until a feeling of intense desire to micturate is registered. The catheter is then removed and micturition is begun. Films are obtained during filling of the bladder, when it is full, during emptying phases, and after completion of micturition to demonstrate the distribution of the residual content of the urinary system.

The X-ray series in cooperative patients demonstrated: (*a*) free reflux through the uretero-vesical junction into ureters which distended to higher than normal calibre; (*b*) complete emptying of the bladder; (*c*) a filling defect in the column of iodide in the ureter occluding the lumen at or near the intramural course; (*d*) the presence, after micturition, of iodide in the ureters and pelves, but not in the bladder. Within two minutes a considerable amount is discharged back into the bladder; further micturition again at this stage empties the bladder and forces some back into the ureters. Repetition of this procedure after a further two minutes completely emptied the urinary tract of residual content.

Furthermore, the emptying of the ureters, as judged by the rate at which iodide is expelled after having been injected into the ureters through a ureteric catheter, is within normal limits. The ureteric orifices in these cases may appear normal, but more often they are larger in dimension and patulous. Obstruction was not a factor.

Of megaureter without reflux only seven cases were available for study. Four patients were females. In six the abnormality was bilateral. The presenting symptoms were recurrent mild abdominal pain or hæmaturia.

Micturition cysto-urethrography demonstrated normal vesical and urethral outlines: no reflux occurred into the ureters, and complete emptying of the bladder was demonstrated.

Emptying times of the ureters were protracted much beyond the normal range of two to ten minutes. In two cases, there was still iodide apparent after twenty-four hours and thirty-six hours, though in one instance the obstruction permitted emptying in approximately twenty minutes. Ureterograms demonstrated a terminal filling defect in the region of the intramural part of the ureter very similar to that seen in megaureter with reflux. Excretion pyelography showed delay in arrival of iodide shadow in the bladder.

The ureteric orifices appeared on cystoscopy to be normal in appearance or to be perched up on a mound. When viewed through the opened bladder, the mound was more easily seen and could be palpated with the fingers. One gained the impression by instrumentation that the orifice initially was smaller than normal, though assessment by cystoscopic catheterization indicated a normal calibre.

Though an actual obstruction is frequently not apparent, the delayed emptying time, in the presence of active peristalsis in the ureter, signifies a definite hindrance to emptying. With the consequent stagnation, urinary calculi are prone to form, as in two of the cases in this series.

In this group, obstruction is definitely present at the terminal end of the ureter. What is the nature of this obstruction? To ordinary tests no organic stricture is apparent, and experiences of surgeons with simple dilatation of the segment of ureter are disappointing. It is referred to by Campbell as achalasia and so far this is probably the best term to use. The surgery of this condition has been marred by subsequent infection that accompanies the vesico-ureteral reflux which follows operations on the uretero-vesical junction.

Management.

Successful management of these two types of cases depends on the ability to remove from the urinary tract the residual urine resulting from the vesico-ureteral reflux. It is the constant intermingling of the fresh urine with the old infected residual content that keeps the infections persisting.

The "triple micturition" procedure is designed to eliminate the residual content. It is possible in cooperative children from about two years onwards. The technique must be learnt and adhered to faithfully. Three separate attempts at micturition are undertaken by these children at two-minute intervals, the whole procedure lasting approximately four minutes. Micturition should be carried out more frequently, by the clock, to prevent the rise in vesical pressure having back pressure effects on the kidney, but the triple micturition procedure need be done only night and morning. This ensures a complete clearing of residual urine twice a day.

In the megaureter with reflux, infection ceases and is completely curtailed so long as the régime is adhered to. Chemotherapy is used at the beginning of treatment for pyuria, though infection can be cleared without this if the régime is learnt quickly.

In babies, reliance must be placed on chemotherapy as cooperation is not forthcoming. If infection cannot be controlled in this way, daily catheterization or even temporary suprapubic drainage may be necessary to drain off the residual urine.

Twelve of these children have now been followed for up to four years, and the control of infection has been most satisfactory by triple micturition. Two children who are mentally backward and three who are under two years of age have been unable to learn the procedure.

Megaureter without reflux can be managed now by conversion into megaureter with reflux. Vesico-ureteroplasty overcomes the obstruction and fractionated micturition eliminates the residual content caused by the reflux.

In order to ensure emptying of the system in these cases, micturition three, four or even five times twice a day is required, depending on the amount passed in the last attempt.

Secondary calculi must be eradicated either at this operation or subsequently.

Triple micturition has other applications, particularly in regard to:

1. Simple test for megaureter with reflux in children with persistent pyuria. The child is asked to micturate

[1] Read at the annual meeting of the Australian Paediatric Association, Canberra, April 21 to 24, 1955.

three times at two-minute intervals. The volumes are measured. If she can successfully pass two or three specimens, it is highly likely that reflux is present. If not, it is unlikely that the abnormality exists. Micturition cysto-urethrography is especially indicated if the response to this test is positive.

2. Reflux which may occur after operations on the ureter, such as operation for impacted urinary calculus in the intramural ureter, and for intravesical ureter after transureteral resection of the ureterocele, and after resection of a simple ureterocele. Triple micturition eliminates the residual content caused by reflux and helps to overcome any infection in these children.

THE WRINGER INJURY.[1]

By DAVID L. DEY, M.B., M.S., F.R.A.C.S.,

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ACCIDENTS form one of the major causes of serious disability and death in children. Injuries of the upper extremities following their being trapped in the power-driven wringer of a washing machine are an increasingly common form of accident, consequent upon the disappearance of the laundress from most homes, and the use of the hire-purchase system. Recently three instances of the condition were seen within a period of four weeks.

The victim is usually a child, but the mother may also be affected. In one of the above-mentioned cases the mother thrust her hand into the wringer to save the child (having forgotten the release handle) and, as is usual, suffered a much more serious injury.

The lesion is typical and its site varies with the age of the patient. (i) In a small child the whole arm is drawn in, and the injury is located in the upper arm, in relation to the axilla. (ii) In a larger child the arm "blocks" at the elbow, and the lesion is found at this level. (iii) In an adult or adolescent the wrist does not pass between the rollers and the injury is confined to the hand.

Fractures are very rarely produced and serious damage is confined to the skin and the subcutaneous tissue. As only one roller of these machines is active, the injury is confined to one surface of the limb, and is a mixture of crush and friction burn. Unless the machine has been released almost immediately, the damage to the skin determines the loss of the total thickness.

The usual "treatment" consists of inactivity whilst a slough declares itself and separates by natural processes. This inevitably leads to infection, and consequent considerable delay in subsequent skin grafting and healing.

The correct line of therapy is to excise all dead tissue and to apply a split skin graft at the earliest possible moment. This can be carried out within a few hours of the injury, provided that the removal of tissue is carried down to the level of the deep fascia, and the graft applied to this. In cases of doubt, or when the arm has been imprisoned for an unusually long time and damage to muscle could conceivably be present, a delay of twenty-four hours will allow accurate assessment at operation of the depth of tissue death. The use of penicillin as a cover during this period is a wise, but by no means essential, precaution.

This approach completely avoids the dangers and difficulties associated with infection, and results in complete healing of the wound within two weeks. The saving in time parallels the preservation of function, and the principle is, of course, applicable to other similar instances of skin damage.

[1] Read at the annual meeting of the Australian Paediatric Association, Canberra, April 21 to 24, 1955.

Reports of Cases.

DIABETES INSIPIDUS WITH A NORMAL DRAUGHT REFLEX.[1]

By CLAIR ISBISTER,[2]

Sydney.

A WORKING knowledge of breast feeding is essential to all pædiatricians whatever their main interest. It is therefore hoped that a few minutes spent studying the physiology of lactation will not appear to you to be a waste of time. Surprisingly little work has been done on this subject, but there are many workers in veterinary physiology and research physiologists studying the secretions of the pituitary and hypothalamus who are beginning to shed light on these mysteries, and as the female of the human species is just another mammal for the purposes of lactation, we may accept their findings.

The maintenance of lactation appears to depend on the suckling reflexes, one concerned with the secretion of milk through stimulation of the anterior pituitary lobe to produce lactogenic hormone, the other with the ejection or let-down of milk through stimulation of the posterior pituitary lobe to produce oxytocin. The failure of either of these will result in failure of lactation, and it is the latter that interests us today in considering a patient with *diabetes insipidus* who was carefully studied during lactation and found to have a normal let-down or draught reflex.

Case History.

Mrs. D. is an alert, intelligent and cooperative patient. She was admitted to hospital suffering from pneumonia when her baby was two months old. She had been fully feeding her baby and she enjoyed breast feeding. She was reluctant to wean the baby and asked if she could express her milk while in hospital, but the amount expressed fell to four ounces a day by the end of the week. She had been conscious of the subjective sensation of the draught occurring occasionally between feeds and after the baby went to the breast, but this had disappeared since her admission to hospital.

She had been treated for *diabetes insipidus* for two years with pitressin tannate, 1·0 millilitre about every forty-eight to seventy-two hours, at the onset of thirst. (She sometimes needed it daily, but at other times could go up to four days without an injection.) At the onset of symptoms, tests had been done to determine the effect of intravenously administered hypertonic saline on an induced water diuresis, and the results of these were consistent with a well-established clinical picture of *diabetes insipidus*, for which no apparent cause was found. There were no other nervous or endocrine symptoms. Her pregnancy and confinement had been normal, but for ten days after delivery she had not needed any pitressin.

It was decided to transfer her to the Royal North Shore Hospital, where the baby could also be admitted, and to attempt to reestablish lactation. The pneumonia appeared to be responding to treatment and she was very anxious to breast feed her child. Breast feeding was recommenced every three hours with complementary feeding. The first day's total was seven and a half ounces, but this gradually increased to 23 ounces in eight days, during which period she felt the draught reflex only once, very faintly. From the ninth to the seventeenth day she noticed that it was occurring once or twice a day after two to five minutes of suckling. It then occurred more frequently and more promptly until by the eighteenth day it was occurring at every feed, one minute after stimulation of the nipple. On the eleventh day after admission to hospital she had had an interlobar empyema drained. The fluid was sterile. As

[1] Read at the annual meeting of the Australian Paediatric Association, Canberra, April 21 to 24, 1955.

[2] Working under a grant from The Royal Australasian College of Physicians.

her condition was very good, breast feeding was continued, one feed only being missed. By the nineteenth day the draught occurred thirty to forty-five seconds after stimulation of the nipple at every feed and only one and a half ounces of complement were taken (Figure I).

This pattern now appeared to be regular, but she continued for the next two weeks to keep a detailed chart and also to record the time when pitressin tannate was given. The injections did not produce a let-down of milk, nor was there any variation in the time lag of the draught in response to suckling.

She was discharged from hospital with lactation reestablished, the baby having only an occasional complement which was soon replaced by the introduction of mixed feeding. The baby had also been very cooperative; it was a sensible, placid baby who used to suck or nibble until milk came, so that, in spite of the uneven milk flow and variable supply, it did not swallow air unduly or fight the breast in impatience.

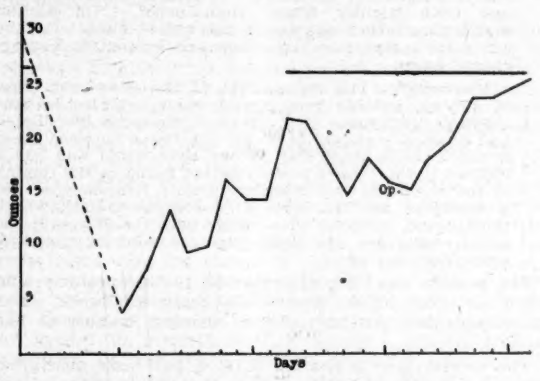

FIGURE I.

Chart showing milk yield during 27 days after patient was admitted to hospital. Horizontal black line indicates the period during which the subjective sensation of the draught was felt. Op. indicates the operation for empyema.

The mother attended the Royal North Shore Hospital pædiatric clinic every month. For a week in each month she kept a record of her draught reflex, and there was no variation in pattern from normal until weaning time, when the time interval between suckling and ejection gradually increased. This first became apparent at the 10 p.m. feed before it was omitted at six months. These observations conform to the normal pattern as described by myself and Niles Newton (personal communication).

Discussion.

The significant features of this case are:

1. This was a moderately severe case of pitressin-sensitive *diabetes insipidus* requiring replacement therapy with pitressin tannate—that is, antidiuretic hormone.

2. Normal labour was followed by ten days without need for replacement therapy. This is a period of normally increased posterior pituitary lobe activity, pitocin being required for uterine involution.

3. Lactation was reestablished after it had almost failed with marked decrease in secretory activity of the breast tissue and in activity of the let-down reflex.

Evidence of the "draught" was subjective only, but this patient proved extremely reliable in her observations; also, having no idea what to expect in her case, I could not in any way influence her by suggestion. As she recognized at once the sensation to which I referred, there was no need to do anything but ask her to record it and to time it. Her observations are exactly similar to those made by a number of normal lactating women in my series and confirmed by Niles Newton in hers.

It appears, therefore, that this patient was unable to produce antidiuretic hormone, but able to produce pitocin for the physiological functions of lactation and labour.

At the present stage of our knowledge it is not possible to explain this phenomenon. Fisher, Ingram and Ranson (1938) state that "in general the intensity of the *diabetes insipidus* is proportional to the degree of interruption of the supraoptico-hypophysial tract" as quoted by Zuckerman (1954). Cross and Harris (1952) and Andersson (1951) have both demonstrated on different experimental animals that stimulation of the supraoptico-hypophyseal tract produces milk let-down, and that section of it interferes with let-down, although Cross and Harris have shown that if the median eminence is intact the reflex can be restored. They have also demonstrated that both oxytocin and vasopressin injections will cause let-down, although oxytocin is much more potent.

The answer may lie somewhere in the work of Bargmann (1949) and Vogt (1953). Bargmann's work shows that the hypothalamus actually secretes a chemical substance that travels down nerve axons; this substance can be stained by Gomori's chrome alum hæmatoxylin-phloxine stain. Vogt has shown that hypothalamic secretion has the same ratio of antidiuretic to pressor substance as posterior pituitary extract, but considerably less oxytocic activity. It therefore appears likely that oxytocin is produced in the posterior pituitary lobe. Whatever the final answer, it appears that there are two different mechanisms for producing these hormones, and in the patient I have demonstrated one mechanism is intact and the other seriously impaired.

Conclusion.

It is only by studying the physiological mechanisms involved in lactation that we can understand the problems of lactation satisfactorily. Failure of secretion has long been recognized. It is hoped that in presenting the detailed study of this case to a group of pædiatricians as a piece of research in physiology of lactation I have stimulated your interest in this aspect of lactation.

Summary.

1. The case is presented of a patient with pitressin-sensitive *diabetes insipidus* who had a normal labour and who established lactation normally.

2. Lactation was seriously disturbed by the onset of an acute illness two months after the birth of her baby. The baby was taken from the breast and the patient expressed her milk.

3. The reestablishment of lactation was studied with test weighing and recording of the occurrence of subjective sensation of the draught reflex and relation of draught to injections of pitressin tannate.

4. It is concluded that this patient can produce oxytocin normally, but is unable to secrete adequate quantities of antidiuretic hormone.

5. Recent experimental work is briefly discussed.

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SPLENOPTOSIS IN INFANCY: TWO CASES.[1]

By S. P. BELLMAINE,
Sydney.

To the ancients the spleen was an organ of mystery and many curious speculations were made about it. A modern minor mystery concerning the spleen is the fact that the present writer, in the last decade, has seen two cases of splenoptosis in infancy, when the condition is indeed a rare one. Rare it is, for in the last quarter of a century, in the records of the Royal Alexandra Hospital for Children, Sydney, there are no cases classified as splenoptosis; and at the Royal Prince Alfred Hospital, Sydney, in the last forty-five years, other than the two cases herein to be discussed, there were only four cases of a movable spleen classified primarily under that heading. In three of these there was torsion of the pedicle causing an acute abdominal emergency. The age of those four patients varied from sixteen to forty-three years.

The first case is one which was reported by the late Dr. Norman Cunningham in THE MEDICAL JOURNAL OF AUSTRALIA, of October 11, 1947. Dr. Cunningham in his report acknowledged that the present writer had seen this case with him. The opportunity is now taken to discuss this already reported case, to add further information concerning it, and to compare and contrast it with the second case which came under notice a little more than a year ago. Cunningham reported his case as "Splenoptosis Associated with Transposition of the Colon". The infant (A.B.) was a female, aged six months, who had been noted to have a distended abdomen from birth. The diagnosis with which the infant was admitted to hospital was "splenomegaly — cause unknown". The present writer recalls his firmly expressed, but incorrect, opinion then held, that the tumour was not a spleen because it was possible to place one's fingers above the swelling, and because it was resonant on percussion. Radiological opinion at this stage was also to the effect that the tumour of the left side of the abdomen was not spleen "because of the position of the gastric and colic gas". Subsequently, however, X-ray examination with a barium enema revealed that:

> The enema flowed freely back to the caecum, passing up the right side of the abdomen, across to the splenic flexure, and then down to the pelvis on the left side. The appearance is that of a transposition of the large bowel.

The blood on examination was found to be essentially normal. Mr. F. W. Niesche then demonstrated that the tumour could be replaced in the normal position of the spleen, splenic dulness thus being restored, and that, all points being taken into consideration, it was probably a "wandering spleen". Cunningham then discussed the case as follows:

> The fixation of the spleen in its normal position is usually determined by peritoneal folds: the gastro-splenic and lieno-renal ligaments which moor the spleen in position, and the phrenico-colic ligament (*sustentaculum lienis*) which supports it from below. The first two form distinct pedicles in a floating spleen, and if the phrenico-colic ligament is abnormal or loose, the spleen, which already moves with respiration and is readily displaced and altered in shape by dilatation of the stomach or intestines, will tend to drop; this stretches the mooring ligaments, and by the pulling on the splenic veins, causes passive congestion of the spleen and enlargement; thus it brings about a vicious circle. The presence of transposition of the colon may indicate an abnormality of the phrenico-colic ligament, which would explain the splenoptosis in this case.
>
> Bohrer describes a case associated with diaphragmatic hernia. Krumbhaar states that the condition may occur in several members of the same family and that the diagnosis depends on the presence of notches, the absence of normal splenic dulness, and the fact that the mass can be returned to the normal position of the spleen.
>
> Splenoptosis may be associated with disease of the spleen, or congenital malformations, or may occur as part of a general visceroptosis . . . . Osler states that the spleen has even been found in the sac of an inguinal hernia.
>
> The risk is torsion, which may give rise to an acute abdominal crisis, and the question of prophylactic splenectomy, although not generally advised in asymptomatic splenoptosis, has been considered in this case. . . . It is postulated that this is associated with an abnormality of the phrenico-colic ligament and transposition of the colon.

The further details now supplied are as follows. When the child was three years of age, she was readmitted to the hospital. She had been suffering from abdominal discomfort and the mass had considerably increased in size. Dr. Cunningham and Mr. Niesche decided that splenectomy should be performed; this was carried out by Mr. Niesche and an enlarged, ptosed spleen was removed. Dr. G. F. S. Davies, on December 12, 1949, reported:

> *Macroscopic*: The specimen consists of a large spleen which weighs 317 grammes. It retains its shape well and feels slightly firmer than usual. On section Malpighian bodies are small but well defined. On the cut surface there are numerous small punctate hæmorrhagic spots.
>
> *Microscopic*: The appearances in the spleen are those of chronic passive venous congestion. There is considerable thickening of the capsule, sinusoids are dilated and unusually plainly seen, but the tissue between these is much more dense and fibrous than usual and has a distinct grain. Many leucocytes are found in the lumina of the sinusoids, but these are mainly lymphocytes, but polymorphs are also present. Fibrous trabeculæ are thicker and, in parts, they merge with the fibrous tissue which separates the trabeculæ. Lymphoid tissue is reduced in amount.

The patient was little disturbed by the splenectomy, and when last seen at the age of six years was well. It is considered that this spleen was enlarged because it had fallen.

The second case is that of R.D., a half-caste aboriginal boy, who at the age of one year and eleven months was admitted to the Royal Prince Alfred Hospital on March 4, 1954. The child had been quite well until he was admitted, the previous Christmas, to a hospital on the north coast of New South Wales, suffering from bronchopneumonia and ascariasis. He responded to treatment for these conditions, and in due course was admitted to hospital in Sydney for "investigation of splenomegaly". On his admission to the Royal Prince Alfred Hospital his father stated that his "stomach had been hard" for nearly a year and that there had been "yellow staining of the whites of the eyes" for two months. The family history was non-contributory.

On admission he was observed to be a dark-skinned child, afebrile, in no distress, and his abdomen was noticeably prominent. An "enlarged spleen" was recorded, as also was the note that there was a "slight icteric tinge to the scleræ". The spleen was in fact recorded as reaching below the umbilicus. It is not surprising that the resident staff reached a provisional diagnosis of "hæmolytic anæmia with splenomegaly". The child was seen by the writer two days after his admission, and the observations were made, firstly, that this child was not jaundiced, and secondly, that although the left-sided abdominal mass had a sharp edge and a notch and was not resonant on percussion, there was no splenic dulness, and one was able to place one's hand above the swelling. It was then demonstrated that the tumour could be pushed up under the ribs, when dulness on percussion was restored, although the viscus was still palpable. The mass was therefore a wandering spleen. A serum bilirubin estimation of less than 0·2 milligramme *per centum* confirmed the opinion that the child was not jaundiced. A blood count which had been made was essentially normal; in particular reticulocytes were less than 0·5%, platelets were 150,000 per cubic millimetre, and there was no spherocytosis or increased fragility of the red cells.

The other child with splenoptosis remained clearly in mind, and therefore a barium enema was ordered. However, the X-ray appearances after the barium enema were

[1] Read at the annual meeting of the Australian Paediatric Association, Canberra, April 21 to 24, 1955.

normal—there was no transposition or abnormality of rotation of the colon. Excretion urography was also carried out, with the result that the pelves and calyces of the kidneys were shown to be normal, and the radiologist (Dr. Green) reported that the "soft tissue shadow on the left side is consistent with a ptosed and probably enlarged spleen".

As the risks of an enlarged, ptosed spleen were considered to be, firstly, torsion of the pedicle, or secondly rupture, either of which would produce an acute abdominal emergency, or thirdly, fixation by adhesions in a grossly abnormal position, with various consequences depending upon the site of the adhesions, it was decided that this spleen should be removed. Mr. Niesche saw the child, agreed with the diagnosis of "enlarged wandering spleen", and agreed to perform the splenectomy for the reasons indicated. The operation was carried out on April 12, 1954. A large, ptosed spleen was removed without difficulty. Mr. Niesche considered that the other organs appeared normal. The child made an uneventful recovery from the splenectomy.

The child's liver was the subject of some discussion. Although it was recorded on the hospital notes on the patient's admission to hospital as an "enlarged liver", it was estimated by the writer, at his initial examination when the wandering character of the spleen was demonstrated, to be one to two fingers' breadth below the costal margin and this was not considered abnormal for the liver in a child of this age. Dr. C. R. B. Blackburn, director of the Clinical Research Unit at the Hospital, requested permission to estimate portal pressure during the operation. The attempt at pressure readings within the gastric veins was not successful, for the reason that these veins were not distended, that is, the portal pressure was not increased. The surgeon did not wish a needle to be placed directly into the portal vein, and he estimated the liver to be normal in size, position and appearance; he agreed to perform a liver biopsy. At the time of operation Dr. Blackburn obtained blood for liver function tests. The results of these were as follows: thymol turbidity 35 units, zinc sulphate turbidity 46 units (normals being less than 15 units).

Because of not unreasonable pressure by his parents for his return home (for they had not seen him since his admission) the child left hospital on May 9, 1954. It was not until May 24 that the final pathological reports on the excised spleen and the liver biopsy material became available. Dr. E. F. Thomson then reported:

> The spleen weighs 365 grammes. The external appearance is normal and on section is firm. The cut surface has a somewhat homogeneous appearance, the Malpighian corpuscles being very indefinite. However, there are some minute white nodules surrounded by darker areas, scattered diffusely over the splenic tissue. The small piece of liver tissue is pale and ? slightly fibrotic. On microscopic examination of the liver; the parenchymal cells are distended with glycogen. The appearances are fairly normal histologically. The spleen, microscopically, shows appearances consistent with a storage disease; special histological stains show stored material to be a lipoid *plus* a muco-polysaccharide, and the pathological diagnosis is, therefore, Gaucher's disease.

This child was a dark-skinned half-caste aboriginal, and no *"café-au-lait"* pigmentation of face, neck, hands and legs, characteristic of the chronic form of Gaucher's disease, was observed or in fact suspected. It is clear that, when the writer dismissed the colour of the conjunctivæ as not being due to jaundice, he overlooked the fact that, despite racial pigmentation, the child's own parents had observed a colour change in the eyes. Brownish pigmentation and wedge-shaped thickening of the conjunctivæ are features of the chronic form of Gaucher's disease. No reference under the heading either of "splenoptosis" or of "Gaucher's disease" to ptosis of the spleen occurring in Gaucher's disease has as yet come to hand. As regards splenectomy in Gaucher's disease, Gross states:

> Although it may be still too early for final evaluation of splenectomy in this disease (i.e. the chronic form of Gaucher's disease) it is our distinct impression that the operation has considerable merit. It could be summed up by saying that, following splenectomy, the abdominal discomfort is relieved, the anæmia is improved, and the physical growth becomes accelerated.

Incidentally, Gross in his book states that in a total of 199 splenectomies performed between January 1, 1931, and September 1, 1952, by himself and his colleagues, only one was done for "wandering spleen", and this was because the organ was already the site of infarction. Nine of those 199 splenectomies were performed for Gaucher's disease. It thus appears that from the point of view of the child's lipoid storage disease, although in the present case the decision to remove the spleen was made on other grounds, it was not an unfortunate decision.

No X-ray examination of the long bones was carried out. A letter dated April 14, 1955, received from Dr. A. A. Hunter reads in part:

> I received your letter this morning . . . . I had not forgotten about R—— D——, but the natives are hard people to contact and I have been unable to X-ray the long bones. Strangely, however, he turned up on Easter Friday with a high fever, temperature 104 deg. and nothing to show for himself, apart from some coarse generalized rhonchi etc. etc. . . . he has not grown much since you saw him, although his father, a reliable person, states that he has been very well. His liver is enlarged one to two fingers' breadth beneath the costal margin. When I carry out the examination of the long bones I will let you know the result.

Summary.

1. Two cases of splenoptosis in infancy are described and discussed.

2. The first spleen appears to have been enlarged because it fell; the second appears to have fallen because it was enlarged.

3. The first case was associated with abnormality in rotation of the colon, and the spleen was the site of chronic passive venous congestion; the second spleen was enlarged by the chronic form of Gaucher's disease, but the present author has seen no other records of ptosed spleens in that disease.

4. Splenectomy may have a place in the treatment of chronic Gaucher's disease; a wandering enlarged spleen is liable to torsion or fixation by adhesions in an abnormal position, for example, to bowel, and splenectomy should therefore be considered before these events have occurred.

5. The diagnosis of ptosis of the spleen is easy if the condition is borne in mind.

Acknowledgements.

Thanks are due to the late Dr. N. C. Cunningham, to Mr. F. W. Niesche, to Dr. C. R. B. Blackburn, to Professor F. R. Magarey, and to Dr. A. A. Hunter, of Macksville, New South Wales, who referred the second case, and to the Fairfax Institute of Pathology at Royal Prince Alfred Hospital.

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Notes on Books, Current Journals and New Appliances.

Clinical Interpreter.

THE correlating in parallel columns of English, French, German and Italian phrases used in dealing with patients results in a most useful little booklet. That the foreign language phrases are not always truly idiomatic, and that many accents have been omitted, are not major faults, since the phrases are intended to be spoken, not written. That in the obstetric section the patient is made masculine (question 352, French) similarly does not matter. There are some inclusions (such as "Is your mother dead?" before

"Of what did your mother die?") and omissions (such as "This might be a case of lead-poisoning" in the midst of purely clinical queries) which could be recommended. However, the idea of the booklet is excellent, and its subject-matter will be of real value, even to those with a schoolboy or scientific knowledge of the languages concerned.

Atlas of Outline Drawings for Vertebrate Anatomy. By Samuel Eddy, Clarence P. Oliver and John P. Turner; Second Edition; 1955. New York: John Wiley and Sons, Incorporated. London: Chapman and Hall, Limited. 11" x 8½", pp. 106. Price: $3.25.

THIS atlas has been prepared for students studying the anatomy of animals commonly dissected in vertebrate anatomy—amphioxus, the dogfish shark, the skull of the sturgeon, the gar and the bowfin, necturus and the cat. The drawings, which are clear and skilfully made, are unlabelled. They are designed more particularly for the student with little drawing ability, as a time-saving aid rather than as a substitute for dissection. They will normally be used in conjunction with a dissecting guide.

Cerebral Vascular Diseases: Transactions of a Conference Held under the Auspices of The American Heart Association, Princeton, New Jersey, January 24 to 26, 1954. Chairman: Irving S. Wright; edited by E. Hugh Luckey; 1955. Published for The American Heart Association, New York and London: Grune and Stratton. 10" x 7", pp. 178. Price: $5.50.

THIS volume records the transactions of a conference held at Princeton, New Jersey, in January, 1954, under the auspices of the American Heart Association. The object of the conference was to obtain facts and opinions as a basis for the initiation of a programme of clinical investigation of various therapeutic procedures in patients with cerebral vascular diseases. Fourteen speakers initiated discussions on various aspects of the problem, and members of the conference participated. The whole field seems to have been covered adequately.

Annual Epidemiological and Vital Statistics, 1952; 1955. Geneva: World Health Organization, 11" x 8½", pp. 544. Price: £2 10s.

THIS is a WHO compilation of vital statistics, causes of death classified by ages and sex, and number of reported cases of and deaths from notifiable diseases, for the year 1952. It should serve as a valuable reference book for all workers in the public health field.

British Medical Bulletin.

THE *British Medical Bulletin* for May, 1955, is devoted to a symposium on "Hormones in Reproduction". It opens with an article by E. C. Amoroso and L. H. Matthews on the effects of external stimuli on the breeding cycle of birds and mammals, which discusses light, temperature and psychological factors. The hypophysis appears as a necessary link in the chain of reactions which lead to sexual activation, and the seasonal cycle appears to be conditioned by external environmental factors which excite or inhibit the secretion of gonadotrophin by the anterior pituitary. The neural mechanisms which control reproductive phenomena are next considered, and the symposium then goes on to deal with the biology and chemistry of the gonadotrophins, the endocrinology of the testis, and many other aspects of the biology of reproduction, concluding with discussions of the part played by hormones in human fertility and in fertility in farm animals; in the latter, various practical methods of increasing the yield from flocks, and new work on other possible methods, are dealt with.

Pharmacopœia Internationalis; First Edition; 1955. Geneva: World Health Organization. 9½" x 6", pp. 370. Price: £1 15s.

THE publication of Volume II of the International Pharmacopœia successfully completes a task begun in 1937 under the auspices of the League of Nations Health Organization and carried on since 1947 by the World Health Organization, through the members of the Expert Advisory Panel on the International Pharmacopœia and Pharmaceutical Preparations, and of other specialists.

This volume consists of 217 monographs, 26 appendices, and one annex. It contains, among others, specifications for some of the pharmaceutical preparations introduced into therapeutics during the last few years (for example, penicillin, chloramphenicol, dihydrostreptomycin, oxytetracycline) and for some synthetic substances of growing importance. It also contains monographs on compressed tablets, sterile injections, and tinctures of substances included in Volume I. In the appendices are descriptions of the relevant methods of assay for some of the substances in the volume, and, as in the first volume, a table giving the usual and maximal doses for adults of all the pharmaceutical preparations included. In addition, for certain drugs in both volumes there is a table of usual daily doses for children. Another appendix contains a list of the International Biological Standards and Reference Preparations at present available.

An annex on solutions of cardiolipin and lecithin has been added, in view of the increasing use of these substances in serological tests.

A detailed index to both volumes is included.

Tercer Congreso Venezolano de Cirugia; Organizado por El Capitulo Carabobeno de La Sociedad Venezolana de Cirugia; 1955. Caracas: Prensa Medica Venezolana. 9" x 6½", pp. 802, with many illustrations.

THIS volume records the first part of the proceedings of the Third Congress of the Venezuelan Society of Surgery. It gives the papers read at the plenary sessions on cancer, industrial surgery and anæsthesia, together with the discussions that followed the papers. These papers are of high merit, but are available only to those who read Spanish; there are no summaries in English.

J.A.M.A. Clinical Abstracts of Diagnosis and Treatment, published with the approval of the Board of Trustees, American Medical Association; 1955. New York and London: Intercontinental Medical Book Corporation with Grune and Stratton, Incorporated. 8½" x 5½", pp. 636. Price: $5.50.

THE *Journal of the American Medical Association* considers that its "Medical Literature Abstracts" is one of its most useful and popular features. Having regard to the prime importance of diagnosis and treatment, the journal has now published a selection of its recent abstracts in these fields in a volume which is stated to be the first of an annual series of official journal publications. The abstracts are arranged in sections covering internal medicine, surgery, therapeutics, pathology, physiology and the various specialties; the dates of publication of the originals are mostly during 1954, although there are a few from December, 1953, and as many dated January, 1955. The abstracts are well selected, and appear to give all the essential points of the originals. The index is adequate. Production is excellent.

Refresher Course for Practitioners; Specially Contributed Articles from the Journal of the Indian Medical Association; Volume I, edited by P. K. Guha; 1955. Calcutta: *Journal of the Indian Medical Association*, 7½" x 4½", pp. 380, with many illustrations. Price: Rs. 8s.

The Journal of the Indian Medical Association has produced this volume of 32 special articles contributed between October, 1954, and May, 1955. It opens with "Diagnosis and Treatment of Malaria" by R. N. Chaudhuri, and as would be expected, this is a complete and competent survey of the subject. Keratomalacia, diphtheria, asthma, essential hypertension, and the anæmias follow in that order, and the remainder of the articles are equally well selected and adequately written. The booklet is well produced, up to date, and could be of value to general practitioners anywhere.

German-English Medical Dictionary. By W. O. Goulden, B.A. (Hons.), Dr.Phil.; 1955. London: J. and A. Churchill, Limited. 8" x 5½", pp. 520. Price: 45s.

THE Second World War dealt a heavy blow to scientific medicine in Germany. German medical journals after the war was over took some time to come to life again and the standard of contributions to their pages was not comparable to that emanating from the country before the war. The position is being changed and medical investigators in English-speaking countries are once more looking hopefully to German periodicals. Medical men and women will therefore welcome Goulden's dictionary. It is well printed in Roman type and of such a size that it can be conveniently handled. The study of medical papers by doctors in foreign countries is one of the methods of promoting international understanding and cooperation.

The Medical Journal of Australia

SATURDAY, FEBRUARY 11, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words of phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE CHILDREN'S HOSPITAL AND THE CHILD.

THE setting aside of hospitals for the care of sick children is a comparatively recent practice—a matter of the past century and a half. Before then children were certainly admitted to hospitals for adults, and foundling homes had taken in unwanted children, ill or well, from early Christian times. However, the mortality amongst children in these places was appalling, and it is easy to understand why there was hesitation to bring ailing children together under one roof for medical care—the reputation even of adults' hospitals was bad enough. Another objection was voiced by the English physician, George Armstrong, who was (according to Castiglioni) the first to describe infantile pyloric stenosis. In 1769 Armstrong founded in London the first "Dispensary for the Infant Poor", essentially an out-patient institution, into which he put all that he had; but when some of the friends of the dispensary wished to have a house fitted up for the care of infants who were ill, along the lines of a hospital for adults, Armstrong would not agree. His comment, which was made in 1772 but is highly relevant to present-day thinking about children's hospitals, was quoted by John Fulton in a paper that he read to a meeting of the Section of Pædiatrics at the Australasian Medical Congress (British Medical Association) in August of last year:

> . . . a very little Reflection will convince any thinking Person that such a scheme as this can never be executed. If you take away a sick Child from its Parent or Nurse you break its Heart immediately; and if there must be a Nurse to each Child what kind of an Hospital must there be to contain any Number of them? Besides, as in this case, the Wards must be crowded with grown Persons as well as Children must not the Air of the Hospital be thereby much contaminated? Would not the mothers or the nurses be perpetually at variance with one another if there was such a number of them together? Would not the children almost constantly disturb each other with their crying? Supposing only a few in one ward should be taken ill of a vomiting and purging, to which infants are so very subject, would not this presently infect the air of the ward and very probably communicate the disorder to other children confined there? Yet this is one of the principal diseases where an hospital might be of service to infants, were it not for insuperable objections just now mentioned. Add to all this it very seldom happens that a mother can conveniently leave the rest of her family to go into an hospital to attend her sick infant.

The problems raised by Armstrong are still not fully solved today, and certainly his views (or at least their negative effect) prevailed at the time. Eighty years passed before the first children's hospital in London was founded. It was in 1852, according to Samuel X. Radbill,[1] that Dr. Charles West, who had previously conducted the Royal Infirmary for Children in London, succeeded in having 49 Great Ormond Street rented and furnished to accommodate 10 patients. Soon the 10 beds became 20, and further growth followed. A "fever ward" for contagious patients was established with a nurse in charge; an autopsy room was provided for the study of disease, and a dispensary came into being. The teaching of nurses, medical students and practitioners, as well as instruction of the public in the care of children, was carried out from the beginning.

Great Ormond Street was not, however, the first modern children's hospital. That honour, according to Radbill, goes to the *Hôpital des enfants malades* in Paris, which was established by the French Government in 1802 (the tenth year of the French Republic). This was the result of an investigation of the *Hôtel Dieu* of Paris ordered by Louis XVI in 1785 because of the deplorable conditions there—conditions which, in fact, were common to all hospitals of the day. The investigators found "a hundred or more patients penned in a ward. Often eight or nine children were heaped in a single bed. Measles, smallpox, malignant diarrheas, and scabies were crowded together in each bed, children and adults in the same overcrowded ward". Two important recommendations appeared in the report: first, each patient should have an individual bed; second, the children should be separated from the adults. Louis XVI had long since lost his head, but the Republic was guided by his appointed investigators, and a 300-bed hospital came into being for children between the ages of two and fifteen years with every kind of acute disease and most of the chronic diseases. The contagious disease wards were well separated from the rest, but warnings against mixing patients suffering from contagious diseases with other patients were soon forgotten, with the inevitable results; an adequate understanding of contagious diseases had to wait for a much later day. However, the *Hôpital des enfants malades* became a notable investigating and teaching centre.

The second of the modern children's hospitals, the Nikolai Hospital for Children in St. Petersburg, was founded in 1834. The third was St. Anne's Children's Hospital of Vienna, which was opened in 1837. Many others had appeared in Europe before the Hospital for Sick Children in Great Ormond Street opened its doors in 1852. The first children's hospital to appear in the United States was the Children's Hospital of Philadelphia, which was opened in 1855. It was fathered by the Pennsylvania Hospital and was much influenced by the Great Ormond Street Hospital and the *Hôpital des enfants*

[1] *Am. J. Dis. Child.*, October, 1955.

malades. In Australia the (now Royal) Melbourne Children's Hospital was founded in 1870, to be followed by the Adelaide Children's Hospital in 1877, and soon afterwards by the Sydney Hospital for Sick Children (now the Royal Alexandra Hospital for Children) in 1880.

The period of a century and a half during which the modern children's hospital has developed is significant in relation to child welfare; it stands out from the milleniums before it, and its close sees the beginning of major new developments in thought and practice. The place of the child in antiquity was often hard, especially if he was poor or unwanted. Both the Greek and the Roman world accepted infanticide and infant exposure, and the "rescued" child rarely had anything better to hope for than slavery, which was what the law allowed. Among the Romans even the Patrician child had no rights of his own; the father possessed absolute powers over his family, which were all too often exercised harshly. The child of the poor expected little, for even his parents had few rights. Thus, if the lot of the healthy child was hard, that of the ailing child was impossible. In this setting the Christian teaching of the dignity and worth of the child must have sounded strange, and it was not widely accepted in practice even amongst those who later acknowledged its authority. But it introduced a novel element of compassion, which was expressed in foundling houses and laws against infanticide. It is sadly ironical that ignorance of the elements of hygiene made death traps of many of these places of refuge. Only in our own day have scientific knowledge and belated acknowledgement of the worth of the child been combined to provide for the sick child care and management that need not make us ashamed. Now the emphasis is broadening and extending to positive aspects of the child's welfare. Unrestricted visiting by parents of children in hospital is gaining surprising support. Children's hospitals are becoming centres for the study and encouragement of the child's better health, rather than just for the cure of his ills, and professional appointments in the pædiatrics field are made to chairs of child health. Wisdom and compassion are combining to give the child his due. Perhaps at last we are learning to escape the condemnation of the millstone.

Current Comment.

PREMALIGNANT CONDITIONS OF THE CERVIX UTERI: A REPORT FROM COPENHAGEN.

UNTIL there is a simple chemical test on blood or urine, the only certain method of cancer diagnosis is histological. Furthermore, until there is a form of treatment which is as specific for cancer as the antibiotics are in the treatment of infections, we must rely upon surgery and radiotherapy. The success of these forms of treatment depends upon early diagnosis, or if possible recognition of the precancerous state. In the case of the *cervix uteri*, there is often a considerable period prior to the development of overt carcinoma.

The concept of precancerous conditions of the *cervix uteri* dates back to 1896 when de Villiers and Thérèse submitted to the International Congress of Gynæcology in Geneva a case of leucoplakia followed for four months. The microscopic appearances suggested to them the beginning of carcinoma. The advancement of the condition after four months caused them to amputate the cervix. At first leucoplakia was thought to be the important precancerous condition. In 1928, however, Schauenstein demonstrated what must have been carcinoma *in situ*. Gradually the clinical and histological aspects of premalignant conditions became recognized. Some, like Schiller, regarded all such conditions as cancer. In 1928 Hinselmann brought out his well-known histological grading of atypical cervical epithelium.

Routine gynæcological examination may reveal no previous abnormality, as only the vaginal portion of the cervix can be seen. While aids to diagnosis such as Schiller's iodine tests and Hinselmann's colposcope assist only in selecting a biopsy site from the vaginal portion of the cervix, a biopsy must still be taken from the cervical canal blindly either by an apple-coring type of procedure or by curettage. Papanicolaou's cytological technique gives fewer than 2% of false positives and about 10% of false negatives, but it often succeeds where other methods fail. It seems, then, that a combination of all procedures is desirable if precancerous lesions are to be discovered and treated.

For some years, in the Radium Centre, Copenhagen, attention has been given to the precancerous lesions of the cervix, and in a recent supplement to *Acta Radiologica*,[1] Olaf Petersen has undertaken to elucidate the spontaneous course of these epithelial abnormalities, their relationship to a possible development of carcinoma and their symptomatology. There were 539 patients attending the Radium Centre between 1930 and 1950 in whom some form of epithelial hyperplasia in the cervix was demonstrated. Biopsy findings were classified into three groups: simple epithelial hyperplasia (327 patients), epithelial hyperplasia with nuclear abnormalities (124 patients), and borderline cases (88 patients).

Carcinoma developed in only one patient exhibiting simple epithelial hyperplasia, so that such lesions can hardly be regarded as precancerous. The borderline groups contained those cases in which examination of some sections gave rise to suspicion of incipient invasiveness; these correspond to "carcinoma *in situ*". The two groups with nuclear abnormalities are the truly precarcinomatous lesions, and the 212 patients (those in the second and third groups) exhibiting such cervical changes form the basis of Petersen's analysis.

The lesions were all discovered during routine examination for a variety of symptoms, of which bleeding disturbances were the most common, occurring in 72·1% of patients. Contact bleeding, discharge and pain each occurred in about 30%. The only significant symptom was post-coital bleeding. A history of pelvic disease, usually inflammatory, was present in 98 (46·2%) of those patients with precarcinomatous conditions. Most patients presented within a year of the onset of symptoms.

Precancerous lesions occurred between the ages of fifteen and seventy-four years. Patients in the borderline group tended to be slightly older than those without suspicion of invasiveness, yet the summits of the histograms each occurred between thirty-five years and thirty-nine years—that is, about ten years before the peak incidence of frank carcinoma.

All but 8·5% of the patients were married or had been married, a marriage rate higher than that for the general population. High parity was not characteristic. Only the first delivery was significant, the number of *nulliparæ* being lower in the precancerous group than among the other patients attending the clinic. No mention of the circumcision rate in Danish males is mentioned in Petersen's analysis, so that other factors than childbirth must eventually be considered.

The objective findings in the 212 patients under consideration were as follows: normal appearance of cervix, 11·8%; simple erosion, 49·5%; suspicious erosion, 30·5%; erosion and leucoplakia, 4·2%; leucoplakia, 3·3%. The clinical appearances were much the same for each histological group.

[1] *Acta radiol.*, Supplement (1955), 127.

The patients who were radically treated when first seen were older, being mostly menopausal or post-menopausal. One of these died from carcinoma of the cervix which must have been present from the start. There were 127 younger patients who were untreated during the entire period. By the ninth year of observation 33% of these had developed carcinoma. By the fifteenth year of observation all patients had either developed carcinoma or reverted to normal. The rate of development of carcinoma followed a straight line till the ninth year, after which there were too few cases to be significant. After the first year, half appeared both clinically and histologically the same, 4% had developed carcinoma, and the remainder had reverted to normal. Carcinoma developed in a shorter period in those exhibiting borderline histological appearances in which incipient invasiveness was suspected. Of the 34 patients who developed carcinoma, the latent period averaged 3·0 years for those in the borderline group, as against 4·1 years for the remainder. In each group the earliest carcinoma was found after five months. Ten could be diagnosed by the microscope, though no clinical suggestion of malignancy was present; 17 were in Stage I, four in Stage II, two in Stage III and one in Stage IV. Of the seven patients in the therapeutically unfavourable stages, five had failed to appear for follow up for periods from two to eight years.

From these figures it is regarded as reasonable to wait a year before resorting to radical therapy, particularly in young *nulliparæ*. This is justifiable, however, only if there are frequent examinations which include biopsies and cytological examinations, for the development of carcinoma in this group was symptomless. When there is doubt as to the cooperation of the patient in follow up, however, more radical procedures are important.

Of those who developed carcinoma, five (14·7%) died, one suffered a recurrence two years after treatment, 26 were symptom-free for periods of one month to eighteen years, and of these seven were symptom-free for more than five years. Two patients were unaccounted for. The total mortality amongst those who were untreated when first found to have a precancerous lesion was 3·9% against 2·4% for those treated immediately.

When surgical treatment of a precancerous lesion is contemplated, simple hysterectomy is preferable to amputation of the cervix. Petersen found that three of seven patients who had amputation of the cervix still had precancerous changes fifteen, ten and four years afterwards. More than half the patients found to have precancerous lesions had either no visible lesion of the cervix or merely a simple erosion. The only symptom of any significance was post-coital bleeding, for it occurred in half those who developed carcinoma, though it was present in one-third of the whole group.

Because clinical examination cannot indicate which patient has a precancerous condition of the cervix, it seems that every gynæcological patient should be examined by cytological and histological methods. Simple epithelial hyperplasia does not *per se* require treatment, but nuclear abnormalities indicate a premalignant condition. As already stated, Petersen holds that radical treatment should not be instituted as soon as the diagnosis is made. Instead, such patients should be followed up at short intervals for about a year to see whether the lesions show a tendency to regress or advance. This is at least open to argument. For all that, the treatise from the Radium Centre at Copenhagen contains valuable material and should be studied by those who deal specially with uterine conditions.

MYASTHENIA GRAVIS.

MYASTHENIA GRAVIS is a relatively common neurological disease characterized by the abnormal fatigability of striated muscle. Typically the disease presents first as weakness of the small muscles after exercise. Usually the face is first affected with ptosis and ocular imbalance as the most common signs. Occasionally the disease is limited to specific muscle groups, but often it is slowly progressive, widespread muscle degeneration takes place, therapy becomes ineffective and palato-pharyngeal involvement and a slow, miserable death supervene. The disease is regarded as metabolic in origin and is possibly associated with abnormalities of the thymus and other glands. There is a specific, dramatic and temporary alleviation of the symptoms when anti-cholinesterases are administered. The standard method of treatment is by the regular oral administration of neostigmine.

In a recent exhaustive symposium[1] the whole problem of *myasthenia gravis* is discussed and the views expressed on ætiology, detection and treatment of the disease show that our knowledge of it is by no means complete. W. L. Nastuk discusses the transmission of impulse at the neuromuscular junction after studies of the membrane action-potential at the motor end-plate. The action of acetyl-choline is probably to increase the permeability of the cell membranes to ions. Positively charged extracellular ions penetrate into the muscle cell, and stimulation to contration takes place.

E. F. von Maanen, in studying the nature of neuromuscular blocking agents, reaches the conclusion that neostigmine is a primary choline esterase inhibitor, and that its action in the myasthenic patient, by actively preventing the destruction of acetyl-choline, is to build up a concentration of the latter to act with the particular receptor mechanism of cell stimulation. Neuromuscular transmission is thus restored.

R. J. Johns *et alii*, after studying the electromyelographic changes found in the myasthenic patient, concluded that the nature of the neuromuscular block resembled that produced by *d*-tubocurarine in the normal subject. This may indicate that the myasthenic state is due to competitive action for the acetyl-choline by choline released by the hydrolysis of the acetyl-choline of prior stimulations.

H. C. Churchill-Davidson and A. T. Richardson studied the effects of decamethonium, which acts in a similar way to acetyl-choline, and produces a depolarizing block in the normal subject. The mildly myasthenic patient is particularly resistant to the depolarizing action of decamethonium. In patients with severe myasthenia, decamethonium causes a block at the neuromuscular junction, but there is no depolarization and there appears to be complete inhibition of the decamethonium. It is suggested that the abnormality causing the myasthenic state is one of alteration in response of the motor end-plate. In patients with mild, localized myasthenia there is resistance of the end-plates to depolarization in the later stages of the disease, the threshold for stimulation is raised and a non-depolarization block ensues. Such a dual response to acetyl-choline itself could account for all the clinical features of *myasthenia gravis*. Comparisons of readings of the electrical and mechanical activity in the myasthenic and in the partially curarized normal subject are described by S. Y. Botelho. These indicate that at least part of the myasthenic abnormality may be due to deficient contractile ability of the muscle itself with neostigmine acting to restore the muscle sensitivity temporarily to normal levels.

A. and H. Wilson report the preliminary findings of the effect of an extract of thymus gland upon animal neuromuscular transmission and voluntary muscle movements. The effect of an extract of thymus from a myasthenic patient was similar to that of decamethonium; that is, the whole extract potentiates the action of acetyl-choline, but an alcohol-soluble fraction has a similar action to the curare drugs. Whether or not these two separate opposed actions are due to more than one substance remains to be elucidated. However, the work so far suggests that the thymus does play some part in the metabolism of the neuromuscular junction. The action of any curare-like substance may be temporarily reversible with neostigmine, but over a period of several years chronic changes at the neuromuscular junction may take place so that subsequent removal of the thymus will be ineffective.

[1] *Am. J. Med.*, November, 1955.

L. M. Eaton and O. T. Clagett discuss the results of thymectomy in their own series at the Mayo Clinic and compare these results with those of others. Of 121 patients with *myasthenia gravis* whose thymus gland was removed by the authors, eight died within three days of the operation. The operative risk is thus high, and the value of the operation must be carefully weighed for each individual patient. Thymectomy for the removal of a thymoma carries an even higher mortality. The conclusions reached are that thymectomy is of value for the young female patient with a comparatively short history of *myasthenia gravis* and in the absence of a thymoma. The onset of normal remissions clouds the results, but of the young women who survive the operation, more than half have a very good chance of attaining a satisfactory remission of symptoms. The value of thymectomy in the male has not been demonstrated.

N. S. Shlezinger reports the effect of pregnancy in the myasthenic patient. Neonatal myasthenia is found only infrequently in the infants of affected mothers; in the babies who survive, a spontaneous and permanent remission occurs. Congenital *myasthenia gravis* in the infants of normal mothers is very rare. The syndrome of neonatal and temporary myasthenia is possibly due to the placental transference of a curare-like substance. In the mothers themselves, pregnancy is usually accompanied by a remission in symptoms at some time. Labour is uneventful, provided the usual treatment of the myasthenia is maintained.

The effects of endocrine extracts on the disease have been studied by C. A. Kane. The results indicate that cortisone had no place in the treatment, but that corticotrophin produces a temporary exacerbation followed by a temporary remission. The administration of corticotrophin may not be a useful form of therapy, but a study of its mode of action may shed further light on the complex riddle of the myasthenic condition.

R. S. Schwab and K. E. Osserman find respectively that WIN8077 and pyridostigmine bromide have some advantage over neostigmine, in that the action of these substances is more prolonged, though the side effects are not materially reduced. Neither seems likely to be the answer to the need for a safe, long-lasting drug to which resistance will not develop. *Myasthenia gravis* is a curious and complex disease. Workers in the field of research are by no means agreed on the explanation of the cause of the neuromuscular failure. However, it seems almost certain that the thymus is involved in the abnormal process, though whether the action is to circulate a curare-like substance, whether acetyl-choline is prematurely destroyed or whether the defect lies in the excitability of the receptor, are still possibilities without the firm framework of a probability.

EFFECTS OF MALARIA CONTROL.

A GREAT DEAL has been written about the depressing effects of chronic malaria on the populations of tropical countries, but most of it has been based on assumption, and although the conclusions reached are almost certainly correct, it has not been possible to make any large series of controlled observations until recently. Now the newer drugs and techniques have made absolute control possible. There is no doubting the direct organic effects of acute and chronic malaria—their assessment is a matter of simple observation. It is the remote, more or less intangible effects that need to be subjected to controlled scrutiny. In countries where malaria is endemic, by the end of the second decade of life the physical signs of chronic malaria have become well established. Concurrently the previously bright child has become progressively slower; he learns less readily and forgets more easily. From then on there develops an apparent physical and mental sluggishness, the susceptibility to general illnesses seems to be much greater, the onset of old age comes prematurely, and the expectation of life is very short. These effects are usually assumed to be due to chronic malaria—whether to chronic toxæmia, or to chronic hypoxia consequent on an anæmic circulation embarrassed by an enlarged and fibrosed spleen, or to innumerable minute areas of fibrosis in all tissues caused by repeated attacks of falciparum fever, nobody ventures to say. But what if they are due to some racial characteristic, or to the remote effects of some kwashiorkor-like damage to the metabolic processes of the liver, not even malarial, but dietetic in origin? A start has been made to investigate some of these possibilities by E. G. Holmes, M. W. Stanier and M. D. Thompson;[1] they have been estimating the serum protein patterns of four groups of Uganda natives and of Europeans living in Uganda. In all groups of natives the pattern differed materially from that of the Europeans, in that the natives had a higher level of total serum protein, their serum albumin level was lower and their γ globulin was higher. But there were significant variations among the four groups, not apparently due to variations in diet, but possibly related to the varying degree of malarial infection which each group suffered. Roughly, the greater the exposure to malaria, the lower the serum albumin level and the higher the γ globulin level. These variations were found among both children and adults. Why such variations should occur, and whether they have any effect on the body's economy, or are themselves the effect of disturbances due to chronic malaria, are matters for further investigation.

Of more immediate practical value, though so far only confirming known facts, is a preliminary observation by M. J. Colbourne[2] on the effects of suppressing malaria with pyrimethamine and amodiaquine in seven-year-old children at a school in Accra, on the Gold Coast. In the course of a year the parasite rate fell from 59% to nil, and the spleen rate from 38% to 4%. There was a small but not statistically significant reduction in liver enlargement. There was a reduction of 50% in absences due to sickness from all causes; 3·3% of the treated children suffered from attacks of malarial fever, as contrasted with 20% of the control group. The treated children showed a slight but not statistically significant advantage in weight increase over the controls. As would be expected, there was no difference in intelligence or mentality between the two groups at the end of the year. This experiment has been too short so far to allow any new conclusions to be reached; if it could be followed through for ten more years, the children would then be eighteen, which is about the crucial age, after which the various degenerative changes begin to appear. Only thereafter would it be possible to compare the effects of malaria in the control group with the condition of those in the treated group. If conditions permit, it is to be hoped that this experiment can be carried through; the final observations would certainly be of the greatest value.

THE SYNDROME OF ALICE IN WONDERLAND.

IT comes as a shock to find the delightful peculiarities of Alice used as evidence that Lewis Carroll suffered from a peculiar nervous syndrome associated with migraine. It is well known that he suffered from migraine. J. Todd has described[3] what he calls the Alice in Wonderland syndrome which in complete or partial form appears in the course of a variety of disorders such as migraine, epilepsy, cerebral lesions, intoxication with phantastica drugs and schizophrenia. It will be remembered that Alice sometimes became remarkably tall or remarkably short. Sometimes the changes were of a more subtle character. At other times she addressed herself as though she was two people and was puzzled about her identity. In the technical jargon of the psychiatrist she had feelings of hyperschematia, hyposchematia, derealization, depersonalization and somatopsychic duality. Other symptoms occurring in the syndrome are illusory changes in size, distance or position of stationary objects in the

[1] *Trans. Roy. Soc. Trop. Med. & Hyg.*, July, 1955.
[2] *Ibidem.*
[3] *Canad. M. A. J.*, November 1, 1955.

subject's visual field, illusory feelings of levitation and illusory alterations in the sense of the passage of time. In the migraine subject these symptoms may appear without or with the usual symptoms of migraine, and are probably quite common. Case histories can be found in neurological literature which note these symptoms very clearly and Todd cites several. He gives details of six cases of his own, four of the patients with migraine and two with other nervous conditions not well defined. Patients never lose sight of the illusory nature of their feelings, but they may be vivid enough to make the subject look in a passing mirrow or shop window. The nature of the symptoms suggests strongly to Todd that their site of origin is the parietal lobe. Experiments which have been done in electrically stimulating the parietal lobe of conscious persons have produced similar symptoms. The infrequency of reference to the symptoms associated with the syndrome in the literature is explained by the reluctance of the patients to discuss symptoms so far removed from normal experience, or the patient may not think the symptoms are worth mentioning. The only importance of the syndrome is that if the examining physician does elicit its presence he can lessen the anxiety of the patient by assuring him or her that the symptoms are not the prelude to insanity. Todd writes: "The revelation that Lewis Carroll (Charles Lutwidge Dodgson) suffered from migraine arouses the suspicion that Alice trod the paths and byways of a Wonderland well known to her creator." Writers with imagination apparently have reason to tremble when psychiatrists study their flights of fancy. When we read of Alice's hyperschematia, hyposchematia, derealization, depersonalization and somatopsychic duality, we wonder what would be the jargon equivalent of a psychiatric study of some psychiatrists. Of course, anyone who appears to resent psychiatric discussion of Alice may himself be the subject of some syndrome with a long name. A comforting thought!

PREVENTION OF RHEUMATIC FEVER.

AT a symposium held in Canberra by the Australian Pædiatric Association on the subject of rheumatic fever in childhood, published in this issue, evidence for the role of hæmolytic streptococcal infection in the ætiology of this disease was presented. The early recognition and adequate treatment of streptococcal infections in all individuals as a means of prevention of rheumatic fever in the susceptible child were stressed. It was agreed that penicillin, which is bactericidal, was the antibiotic of choice. The sulphonamides, being bacteriostatic, were much less effective in the therapy of streptococcal infections.

At least one recurrence of rheumatic fever was noted in fifty-one of a series of eighty-six patients observed in Sydney over a ten-year period and recently reviewed at the Institute of Child Health. No child in this group had received continuous prophylaxis against streptococcal infection. This experience was in keeping with that published overseas.

A corollary to these arguments is the need for continuous protection of the rheumatic child from recurrent streptococcal infections. The evidence for the prevention of recurrent episodes of rheumatic fever by the continuous oral administration of small doses of sulphonamide throughout the year is now overwhelming. The place of penicillin, orally administered, as a prophylactic agent is becoming clearer. Experience gained at the Institute of Child Health, Sydney, over the past three years tends to confirm the favourable reports, already published elsewhere, of its efficacy. Further studies on a long-term basis are necessary before a more definite statement can be made. The theoretical advantages of penicillin as a prophylactic agent over the sulphonamides are balanced by the need for its administration in the fasting period between meals and the cost to the patient.

There is, however, no doubt that the early and adequate treatment of streptococcal infections with penicillin in all individuals and the continuous daily administration throughout childhood of prophylactic doses of sulphonamides for the known rheumatic patient are of much greater importance than any other measures at present available for the prevention of this disease and of its recurrences.

IMMUNIZATION AND PARALYSIS.

THE administration of immunizing doses of active sera may, in the susceptible individual, be followed by a reaction varying between local soreness, general malaise and alarming anaphylactic shock. The reactions are fortunately mostly mild, and recovery is usually complete. Very occasionally are seen fit young persons in whom there is localized flaccid paralysis of muscles, either in the arm or extending out in a scapulo-humeral type of distribution. The onset is sudden and apparently inexplicable. The patient is usually well at the time, though there may be a history of classical serum sickness after the injection. He may notice no more than a weakness of the supraspinatus or of the deltoid. The lesion is found particularly in service recruits at the commencement of their training, and the signs are usually confined to the limb into which the inoculation was made. The nature of the disability is a form of motor neuritis, and recovery is often incomplete. The exact cause of the lesion is unknown, but the immunization is undoubtedly the primary factor. Cases have followed immunization against tetanus, typhoid-paratyphoid, pertussis, diphtheria and rabies.

H. G. Miller and J. B. Stratton[1] describe four main types of the clinical syndrome. The most common is radiculitis, sometimes involving the brachial plexus, and associated in the acute stage with severe referred neuritic pain. Other forms are polyneuritis with loss of sensation and even the Guillain-Barré syndrome, myelitis or Landry's paralysis, or even cerebral and meningeal types with acute disseminated encephalomyelitis.

The lesion is seen most commonly two or three weeks after the mass inoculation of service recruits with combined T.A.B. and tetanus toxoid. It may be rather more common than is thought, for some patients with mild brachial radiculitis may not complain of the illness, and even when they do so confusion with poliomyelitis or a cervical disk syndrome may occur. Certainly if large groups of inoculated men are examined, the occasional man with very mild asymptomatic Erb-Duchenne scapulo-humeral paresis will be discovered. J. B. MacGibbon[2] reports the results of a review of 360 patients admitted to the Johns Hopkins Hospital with a diagnosis of serum sickness. Six of these patients had neurological signs. MacGibbon suggests that of isolated muscles, the *serratus magnus* is the most commonly affected. Differential diagnosis from several peripheral and central nervous diseases is sometimes possible only on the history of the association with recent immunization. The lesion is probably one of vascular change in the nutrient vessels of the nerve associated with œdema of nerve and nerve roots. The fifth and sixth cervical roots seem to be the most susceptible to the neuritis.

Treatment follows the same pattern as in other diseases of the lower motor neuron type. In following the progress of repair in the more severe lesions, considerable information can be obtained by the electromyelographic study of affected neuromuscular junctions. Unless the complex potentials of recovery are found within a few weeks after the inoculation, the prognosis is likely to be poor.

[1] *Quart. J. Med.*, January, 1954.
[2] *Am. J. M. Sc.*, November, 1955.

Abstracts from Medical Literature.

MEDICINE.

Chemotherapy and Vanishing Lungs.

I. RAPPAPORT (*J.A.M.A.*, August 20, 1955) describes a condition in which lung lesions, especially tuberculous, healed under chemotherapy, especially isoniazid and streptomycin, leave areas in which the lung tissue appears to have disappeared. These areas appear to be airspaces, and are often called cyst-like cavities. The changes were observed before chemotherapy was introduced. The condition has been considered as due to emphysema. It is said that these cyst-like areas, if due to healed tuberculosis, may be later a focus for a flare-up of the infection. The author suggests that such areas should be removed surgically.

Smoking Deterrent.

G. W. RAPP *et alii* (*Am. J. M. Sc.*, July, 1955) discuss a critical evaluation of a lobeline-based smoking deterrent. They state that lobeline has long been used as a deterrent to smoking, but that its side effects were almost as bad as the effect of tobacco. The authors used lobeline sulphate combined with a fast-acting antacid such as sodium bicarbonate or aluminium hydroxide, together with a slow-acting antacid such as aluminium trisilicate or magnesium carbonate. Two milligrammes of lobeline sulphate were combined with 100 milligrammes of a mixture of slow-acting and fast-acting antacid, and given once daily. Subjects treated in this way reduced their daily number of smokes to a considerable extent, but mainly for a short period only.

Fluorocortisone Acetate.

T. B. FITZPATRICK *et alii* (*J.A.M.A.*, July 30, 1955) describe sodium retention and œdema resulting from the percutaneous absorption of fluorocortisone acetate. They state that it had been observed that topical application of hydrocortisone for dermatitis sometimes resulted in alleviation of areas of dermatitis distant from the area of application. In one woman with atopic dermatitis treated with fluorocortisone acetate (0·2%) generalized œdema occurred, and now five more similar results are reported. In most cases the lotion was applied three times daily, with benefit in relation to the skin lesion; but when œdema occurred, the application of the lotion was reduced to once daily. The œdema subsided in all cases. Decreased sodium excretion was noted while the œdema persisted.

Chlorpromazine in the Management of Tetanus.

A. C. E. COLE AND D. H. H. ROBERTSON (*Lancet*, November 19, 1955) have found that in six cases the combination of chlorpromazine with phenobarbitone sodium in adults, and with chloral in children, controlled tetanic spasms for eight to twelve hours, but not for longer. The patients' anxiety—a notable feature in tetanus—was replaced by euphoria. The authors state that not enough patients have been treated to show whether chlorpromazine reduces the mortality from the disease. But there is no doubt that it spares the patients much of the acute mental anxiety and physical pain and exhaustion due to the spasms; and the regime does not make inordinate demands on the medical and nursing staffs.

Excretion of Radioactive Iodine in Human Milk.

H. MILLER AND R. S. WEETCH (*Lancet*, November 12, 1955) state that the amount of iodine excreted in human breast milk has been estimated at 15 to 150 microgrammes per kilogram. They have found that ^{131}I is concentrated in human milk to such a degree that a drink of 25 microcuries given to a nursing mother may have an adverse effect upon the infant's thyroid gland. They recommend that radioactive iodine should not be given to a nursing mother, and draw attention to the fact that radioactive iodine tests may be left largely in the hands of technicians, who cannot necessarily be expected to appreciate the biological risks involved.

Large Lung Sections as Teaching Instruments.

A. J. BLANCHARD (*Dis. Chest*, August, 1955) describes how sections, 400μ in thickness, of an entire lung, gelatin-embedded and frozen, may be cut and mounted unstained on filter paper. An attractive preparation is obtained when the sections are sprayed back and front with an aerosol of plastic material. It can be handed round a class of students for viewing by reflected or transmitted light and can easily be kept clean.

Prostatic Obstruction following Treatment with Isoniazid.

G. H. BLENNERHASSETT (*Dis. Chest*, September, 1955) reports four cases in which the administration of isoniazid appeared to cause a syndrome of prostatic obstruction. It is suggested that the danger of such a complication may be greater in elderly patients and in those with poor renal function. One of the patients, eighty years of age, had received 200 milligrammes of isoniazid daily for six weeks; and two others aged seventy-nine and seventy-seven years, had received 300 milligrammes a day. This was also the dose received by the fourth patient, aged thirty-eight years, who suffered from diabetes and who had albumin, blood cells and casts in the urine.

Endocardial Fibroelastosis.

J. J. KEMPTON AND L. E. GLYNN (*Quart. J. Med.*, N.S. 24: 191, 1955) report three cases of endocardial fibroelastosis with associated valve abnormalities. They state that such cases are likely to present in infancy with the more gradually developing manifestations of cardiac failure, often without other evidence of heart disease. Differentiation from technical feeding difficulty and respiratory infection may be very difficult. Digitalis has proved beneficial in treatment; and because of the possibility that the disease may not always be fatal, its use is encouraged. The pathogenesis of the disease is discussed in detail.

Obesity in Childhood.

O. H. WOLFF (*Quart. J. Med.*, N.S., 24: 109, 1955) studied 100 obese children at the Children's Hospital, Birmingham. Their birthweights were not above average. They were, on an average, taller than normal socially grouped children, with the exception of those from the professional class. During a period of rapid weight reduction, the obese children showed less than the expected gain in height. The onset of puberty occurred about one year in advance of normal average children, but only six months in advance of normal tall children. Evidence is adduced that both tallness and the early onset of puberty in obese children are the results of overeating.

Diabetic Glomerulosclerosis.

A. T. LAMBIE AND A. MACFARLANE (*Quart. J. Med.*, N.S., 24: 125, 1955) report a clinico-pathological study of 120 patients with diabetes. Glomerulosclerosis was found in 45% of cases. Mild glomerulosclerosis is clinically silent, and may remain so when it becomes severe, especially in elderly diabetics. Only 11 patients had albuminuria and nephrotic œdema. The authors suggest that the severity of the renal lesion is related to the duration of diabetes and its degree of control, but not to its severity. They found that the average duration of the diabetic state was 11·7 years in those patients with evidence of glomerulosclerosis, and 7·3 years in those patients with no evidence of the lesion. In most decades the incidence of the lesion is approximately 50%.

Diagnosis of Non-Paralytic Poliomyelitis.

J. B. R. COSGROVE (*Canad. M.A.J.*, June 1, 1955) has analysed the findings in 164 patients followed up after being suspected of having epidemic poliomyelitis. He concludes that analysis of symptoms alone will not aid in the clinical diagnosis. During an epidemic neck rigidity, back rigidity, Kernig's sign, Brudzinski's sign and muscle tenderness are suspicious findings. If the cerebrospinal fluid is normal when the above signs are present, there is less than 3% chance that the patient is suffering from the disease. On the other hand, 6% of patients with abnormal cerebrospinal fluid had no signs except fever. Clinical diagnosis will be missed in these cases unless the cerebrospinal fluid is examined. It is concluded that examination of the cerebrospinal fluid is most valuable in the diagnosis of non-paralytic poliomyelitis.

Lower Œsophageal Pain.

J. H. BAYLIS, R. KAUNTZE AND J. R. TROUNCE (*Quart. J. Med.*, N.S., 24: 143, 1955) distended with a balloon the lower part of the œsophagus of eight normal subjects and three patients with coronary disease. This led to spontaneous and rhythmic œsophageal contractions, together with retrosternal discomfort, which increased during the contractions. The sensation

provoked by this manœuvre was of fullness or distension rather than the oppression or constriction of coronary disease. When severe, the pain rapidly reached a climax and then rapidly abated in from ten to thirty seconds. Its distribution was similar to that of *angina pectoris*, but was not associated with changes in the electrocardiogram. The pain and the contractions were frequently inhibited by amyl nitrite, but not by atropine. It is concluded that both subjectively and objectively lower œsophageal pain differs from cardiac pain.

Carbon Dioxide Narcosis.

E. K. WESTLAKE, T. SIMPSON AND M. KAYE (*Quart. J. Med.*, N.S., 24: 155, 1955) review the clinical and biochemical findings in 16 cases of carbon dioxide narcosis. Fourteen of the patients already had chronic bronchitis and emphysema, and two had asthma. They were being treated with oxygen therapy during an acute respiratory disturbance when narcosis occurred. Carbon dioxide narcosis is characterized by mental disturbance, ranging from confusion, mania or drowsiness to profound coma, and is associated with headache, sweating, muscle twitching, raised intracranial pressure and occasionally papillœdema. Mental disturbance was usually present when the pH of the plasma was less than 7·2 or when the carbon dioxide tension in the arterial blood was greater than 100 millimetres of mercury. Coma usually supervened when the pH fell below 7·1 or the carbon dioxide tension rose above 120 millimetres of mercury. Most patients were conscious if the pH was above 7·3 or the carbon dioxide tension was less than 80 millimetres of mercury. The authors suggest that in the prevention and treatment of carbon dioxide narcosis, oxygen should be given in slowly increasing concentration by nasal catheter or face mask starting with one to three litres per minute. Respiratory stimulants and other measures designed to improve ventilation and effective gas exchange should not be neglected.

Reduction of the Serum Cholesterol Level.

J. M. BARBER AND A. P. GRANT (*Brit. Heart J.*, July, 1955) have administered sitosterol, a plant sterol, incorporated in biscuits, to patients with coronary arterial disease, cardiac ischæmia and a raised level of the serum cholesterol. They have observed a rapid and consistent fall in the level of the serum cholesterol, but not either in the total lipids or in the neutral fat of the blood. One patient died as the result of further infarction of the heart, notwithstanding that his serum cholesterol level had been reduced.

Emphysema and Diffuse Fibrosis of the Lungs.

R. D. MILLER *et alii* (*Dis. Chest*, September, 1955) have conducted experiments to determine the relative value of intermittent, positive-pressure breathing and the inhalation of bronchodilators in aerosol form in the treatment of pulmonary emphysema and diffuse fibrosis of the lungs. It was found that neither form of treatment altered the basic pulmonary lesion. Patients in whom there was fibrosis of the lungs, with minimal evidence of bronchospasm or other obstructive features, were not improved by the two treatments in combination. The intermittent positive-pressure breathing without the use of the bronchodilators proved unsatisfactory, but the two in combination were helpful to a majority of the emphysematous patients. Persistent objective improvement in respiratory efficiency was unusual and, when it occurred, was thought to be due to improved bronchial hygiene following bronchodilatation.

Chest Pain in Respiratory Alkalosis.

B. P. WOLFF (*Dis. Chest*, September, 1955) discusses the syndrome of hyperventilation with alkalosis. He attributes to the alkalosis certain symptoms, such as pain in the chest, lassitude and faintness, which are commonly ascribed to emotional disturbance. He believes that the chest pain arises in the tendinous insertions of the diaphragm and that it is due to prolonged stretching and atony. Treatment consists of acidulation with ammonium chloride, reassurance, mild sedation and outdoor exercise in the form of long walks. This last is found to be difficult to enforce because of the complaint of fatigue; but it is to be explained that exercise reduces tension, replenishes the carbon dioxide, and strengthens the diaphragm. If the patient can be persuaded to take but a few long walks, he is gratified by the relief of symptoms experienced.

Early Diagnosis in Phlebitis of the Leg.

T. ORTIZ-RAMIREZ AND R. SERNA-RAMIREZ (*Am. Heart J.*, September, 1955) describe a new method for the early diagnosis of phlebitis of the lower limbs. They claim that this method is more reliable than Homans's sign. With the patient in the recumbent position and with the limb to be tested slightly flexed, a sphygmomanometer cuff is applied above the knee and inflated to a pressure of about 40 millimetres of mercury. The venous hypertension thus provoked induces, in the presence of deep phlebitis, pain in some place, mostly in the popliteal region or the calf. This pain increases during five minutes, sometimes equalling in intensity the spontaneous pain that is usual in these cases, and disappears as soon as the pressure is released. Unless the pain appears, increases with the pressure and disappears as described, the "sign" of phlebitis is not regarded as positive.

Diagnostic Pneumoperitoneum.

H. G. TRIMBLE AND W. B. LEFTWICH (*Dis. Chest*, September, 1955) recommend the induction of artificial pneumoperitoneum as a diagnostic aid in a variety of clinical situations, as in (i) suspected subphrenic abscess; (ii) lesions of the cardiac portion of the stomach, when the pneumoperitoneum is combined with an opaque meal examination; (iii) the detection of ascites when the amount of fluid is small; (iv) the study of the pelvic organs of adult females; (v) the elucidation of X-ray opacities contiguous to the diaphragm. For the study of the pelvic viscera, the bladder and the rectum are emptied, and from 500 to 1000 millilitres of air are introduced into the peritoneal cavity. The patient is placed prone on the X-ray table with two pillows under the thighs and an air pillow under the epigastrium. The X-ray beam is angled axially through the pelvic canal, and three films are taken directed at 10°, 20° and 35° cephalad. The Potter-Bucky diaphragm is used. The uterus, Fallopian tubes and ovaries may be clearly defined.

Carcinoma of the Bronchus.

E. A. GRAHAM (*Dis. Chest*, April, 1955), writing on the ætiology of bronchogenic carcinoma, points out that a mistake is commonly made in thinking that bronchogenic carcinoma is a single disease. There seem to be at least three separate varieties, each with a different ætiology. The epidermoid or squamous-cell carcinoma is the variety in which there has been a very great increase in incidence of recent years and which is rarely found in a non-smoker. The adenocarcinoma occurs with equal frequency in the two sexes and not infrequently is seen in non-smokers. The alveolar-cell carcinoma is rare and is probably due to a virus.

The Cause of Patent Ductus Arteriosus.

O. M. HARING (*Dis. Chest*, January, 1955) disputes orthodox theories that patency of the *ductus arteriosus* is due either to an arrest of development or to defective oxygenation of the blood during or shortly after birth. She offers evidence in support of a new theory, that premature closure of the *foramen ovale* is the cause of failure of the ductus to close at the normal time. She points out that, except in complex cardiac malformations, patency of the *foramen ovale* and patency of the *ductus arteriosus* do not coexist, also that in newborn infants, with the *foramen ovale* closed, the walls of the patent ductus have been found to be hypertrophied.

Pernicious Anæmia and Cancer of the Stomach.

N. ZAMCHEK *et alii* (*New England J. Med.*, June 30, 1955), reviewing 1222 patients with the diagnosis of pernicious anæmia at the Boston City Hospital, found that about 10% had cancer of the stomach by the time they died or left the clinic. The authors state that this high incidence of cancer warrants the routine use of screening tests.

Cardiac Pain.

D. S. STUCKEY (*Brit. Heart J.*, July, 1955) has studied the cardiac pain which is associated with mitral stenosis and congenital heart disease. The pain was thought not to be due to coronary arterial disease, and the latter was not found in any subject upon whom an autopsy was performed. The factor common to all patients with cardiac pain was a mechanical obstruction to the circulation of the blood; this caused a low cardiac output that did not increase adequately on exertion. The author concludes that cardiac pain, when it occurs in young subjects with rheumatic or congenital heart disease, suggests an obstructive lesion and is an index of severity in those with mitral, aortic or pulmonary stenosis.

Medical Societies.

AUSTRALIAN PÆDIATRIC ASSOCIATION.

THE fifth annual meeting of the Australian Pædiatric Association was held at Canberra from April 21 to 24, 1955, PROFESSOR LORIMER DODS, the President, in the chair. The Association entertained as official guests the Minister for Health (Sir Earle Page), officers of the Commonwealth Department of Health, members of the staffs of the Australian National University and the Institute of Anatomy, and the Editor of THE MEDICAL JOURNAL OF AUSTRALIA.

Annual Report and Financial Statement.

The annual report and financial statement for the preceding twelve months were received and adopted.

Election of Office-Bearers.

The following office-bearers were elected for the year 1955-1956:

President: Dr. Kate Campbell.

Vice-President: Dr. T. Y. Nelson.

Immediate Past President: Professor Lorimer Dods.

Honorary Secretary: Dr. Howard Williams.

Honorary Treasurer: Dr. F. Douglas Stephens.

Executive Committee: Dr. P. A. Earnshaw (Past President, Queensland), Dr. R. Wall (Tasmania), Dr. M. Cockburn (South Australia), Dr. R. Crisp (Western Australia).

Sixth Annual Meeting.

It was decided that the sixth annual meeting should be held at Canberra in April, 1956.

The Pathogenesis of Poliomyelitis.

PROFESSOR FRANK FENNER (Canberra) read a paper on the pathogenesis of poliomyelitis (see page 205).

R. SOUTHBY (Melbourne) asked whether Professor Fenner could tell them the details of the Salk immunization technique. Professor Fenner said that he did not know exact details, but he thought they were weekly subcutaneous injections of one millilitre for two injections and a third at five to seven months. But those things would undoubtedly change. The vaccine itself would be improved with technical improvements in virus production, and he thought that they could anticipate the titre going up 10 to 100 fold in the next few years.

S. WILLIAMS (Melbourne) said that Professor Fenner had helped him a great deal to understand what could be expected from the Salk vaccine. Many would be interested to know that Dr. Bazeley had taken himself to America when he saw the possibilities of tissue culture in work with poliomyelitis. He had worked with Salk and was paid by the Americans. Dr. Bazeley was absolutely "sold" on the Salk vaccine, and Sabin in America and Burnet in Australia had indicated their preference for a live vaccine, but Dr. Williams thought that for the present America's enthusiasm for the Salk vaccine should be followed and that it should be accepted without hesitation for the time being. Dr. Bazeley in a recent letter had reported that they now had a killed vaccine very much more powerful than that used in the large-scale trials. Dr. Williams hoped they would all support the vaccine, for by doing so they should be able to speed up its arrival and use, whatever the channels through which it eventually came.

G. G. L. STENING (Sydney) was interested to hear of varying antigenic response to the vaccine and asked whether the vaccine was tested for potency before release. It seemed to him that immunization by a killed vaccine followed by an attenuated live vaccine should be good, but did he understand correctly that only one strain of attenuated live vaccine was available? If this was so, how long was it likely to be before all strains were available?

Professor Fenner said that one of the advantages of the killed vaccine, in which one had no need to be worried about rapid deterioration of the product, was that it was possible to test potency before release of a batch of vaccine. Each batch was tested for potency, for the presence of live poliomyelitis virus and for the presence of any other viruses. Even so, the batches coming from various large laboratories varied somewhat in antigenic potency. Among the various strains of virus, it seemed that invariably type I grew less well than the others in tissue culture or for some reason was less effective than types II and III. As for the second question, work was going on in many centres with attenuated live virus by using a variety of animals and techniques. Professor Fenner thought that there were available strains of all three types of virus that showed attenuation for the monkey. The only one that had been tried in humans was type II. There was a tremendous amount of work going on, but years of work had still to be done before safe attenuated strains of all three types would be available. However, a killed vaccine that was effective was available. With a killed vaccine, if its virus content was increased, its potency was increased.

A. WILLIAMS (Melbourne) referred to the state of viræmia and the crossing of the so-called blood-brain barrier. He asked if it was known whether the virus crossed at any particular place. He also asked whether spread occurred directly from the blood to various parts of the spinal cord.

Professor Fenner said that it was known that the virus did not go from the alimentary tract along the nerves to the central nervous system. Why and how the virus got across from the blood-stream to the central nervous system in a small proportion was not known. A similar state of affairs existed in the virus encephalitides where only one in a hundred or one in a thousand infected individuals got a central nervous system involvement. That only meant that the problem of spread to the central nervous system was a general and not a special one. Most competent neurohistologists believed that once the virus entered the nervous system intraneural spread did occur.

G. E. J. ROBERTSON (Sydney) asked at what age Professor Fenner suggested that children should be immunized.

Professor Fenner said that in primitive communities children were immunized very young because a lot of virus was circulating and the children ate a lot of it when they were very young. He supposed that the ideal would be to imitate that process with vaccine and to immunize children before they started to mix freely in the community. This presupposed the availability of an adequate amount of vaccine.

PROFESSOR L. DODS (Sydney) asked whether Professor Fenner thought that they could answer Dr. Robertson's question by saying that when sufficient vaccine was available they might commence immunization in the first year of life, perhaps at six months.

Professor Fenner replied in the affirmative.

JOHN COLEBATCH (Melbourne) said that it was their experience that poliomyelitis in a mother at the time of confinement was not uncommon, but paralytic poliomyelitis in the baby was almost unknown. The customary explanation given had been that the viræmic phase of poliomyelitis was very brief or non-existent, but Professor Fenner had shown that such was not the case. Could he offer another explanation? Secondly, since effective immunization to type I had reached only about 63%, what was the relative incidence of type I infections in Australia at present?

Professor Fenner said that he was not acquainted with the actual incidence in the newborn, but drew attention to the infrequency of chickenpox, measles or any of the exanthemata in the newborn, where a similar set of circumstances existed. The only data available in Australia on the strains of virus circulating had been published by Ferris and Thayer. In 1954 it was predominantly type I in Melbourne; in the previous year the whole three types of virus had been found. Type I was the least effective in the American trials. The vaccine available now might be much better than that available a year previously. He thought that the history of the production of poliomyelitis vaccine would be much like that of penicillin; the yield might rise a hundredfold or more.

E. STUCKEY (Sydney) asked whether if the new vaccine gave protection for only a short time, Professor Fenner would advocate its widespread use in the absence of an epidemic.

Professor Fenner said that one had to consider other accepted procedures. Even smallpox vaccination was regarded, in areas where smallpox was endemic, as a temporary protection, and in the Dutch army in the Dutch East Indies vaccination was carried out each year. In B.C.G. vaccination they did not know that the protection conferred lasted for more than a couple of years, but it was thought to be a worthwhile procedure. In Australia since the War, the three types of poliomyelitis virus appeared to have been circulating all the time. Certainly from Melbourne studies one gained the impression, not of violent epidemics, but of a constant low endemicity of all types of virus with occasional peaks of disease incidence.

F. W. CLEMENTS (Sydney) asked whether, if they waited till an epidemic occurred, the time required for immunity to develop after vaccination might be too long to have an effect on that epidemic.

Professor Fenner said that he thought that was quite true. By the time an epidemic was recognized, the amount of circulating virus was very large. Any vaccinating programme at that stage would take time to carry out, and this factor, too, would make the programme too late to affect the epidemic.

John Colebatch asked whether any poliomyelitis had been attributed to the vaccine in the American trial.

Professor Fenner replied in the negative; he said that the statement had been made that none was.

Professor L. Dods said that he understood that a hamster given an intramuscular injection of cortisone was much more susceptible to experimental infection with poliomyelitis vaccine. If this was an established fact, was there a hazard of this type for the child receiving intensive and prolonged cortisone therapy during an epidemic of poliomyelitis?

Professor Fenner said that Bodian's work, which resulted in the study of the provoking effect of inoculations, had started out to examine the effect of cortisone on poliomyelitis in monkeys. He had not found any increase, but he had noted increase in paralysis and localization in the injected limb due to the inoculation of that material.

Professor Dods asked why Salk had not used an adjuvant vaccine, virus *plus* paraffin *plus* a dispensing agent. Professor Fenner said that Salk had set out to develop such a vaccine, which in animals gave greater protection than a saline suspension vaccine. Then the people interested in cancer had pointed out that the adjuvants might prove to be a cancer hazard, but whether it was would not be known for twenty years. So Salk had turned to saline vaccine and was surprised and pleased to find he could obtain a satisfactory antibody response with three inoculations of such preparations.

A Symposium on Rheumatic Fever.

The opening paper to a symposium on rheumatic fever was presented by PROFESSOR H. K. WARD (see page 208).

M. L. POWELL (Melbourne) read a paper entitled "Four Facets of Rheumatic Heart Disease in Pædiatrics" (see page 210).

BRYAN DOWD (Sydney) presented a short paper entitled "Some Aspects of the Natural History of Rheumatic Fever". He stated that the paper was based on the experience which he had gained as one of a team working on some of the problems of the disease at the Institute of Child Health, Sydney. The first difficulty that faced anyone working in the field was diagnosis. The diagnostic criteria, laid down by Duckett Jones in 1944 and later modified by the International Committee studying the effects of salicylate and hormone therapy, had been a great advance. These criteria had allowed of the standardization of results in the various centres where the disease was being studied.

Three hundred and sixty-three patients admitted to the Royal Alexandra Hospital for Children, Sydney, between 1935 and 1954 had recently been studied. The history of each patient's illness had been carefully reviewed to ensure that the diagnostic criteria had been satisfied and each patient had been recently examined.

Diagrams were shown to illustrate the following points:

1. Age incidence at initial episode of the disease. Of the 363 patients, 40% were less than six years old at the onset of the disease, 37% between six and nine years, and 23% between nine and thirteen years.

2. Sex incidence. The sex incidence was equal for males and females.

3. Incidence of major manifestations. The 363 patients had suffered some 627 episodes (or "attacks") of the disease. The 627 episodes were analysed. In 81% carditis was present, in 76% arthralgia, and in 19% chorea. Nodules were noted in 5% and *erythema marginatum* in 3%.

4. Recurrence rate. "Episode" and "recurrence" were defined. Analysis was made of 86 patients who had suffered an initial episode of rheumatic fever between 1935 and 1944, and thus had been observed over a period of ten years. The period of maximum risk of recurrence was found to be within the first five years after the initial attack of the disease, with a peak recurrence rate at two years. This suggested that if the aim of prophylaxis was the prevention of recurrences, prophylaxis should be continued for at least five years after rheumatic fever was diagnosed.

4. Ten-year prognosis. Analysis was made of the extent of cardiac involvement in each of the 86 patients who had been observed over the ten-year period and had received no continuous prophylaxis. Of these, 10% were dead, 19% were judged to have severe rheumatic heart disease, 19% had milder rheumatic heart disease, and 52% were considered to have "potential" rheumatic heart disease.

Dr. Dowd concluded by emphasizing the preliminary nature of the report, which, he said, had been gathered together for the purpose of presentation to the Australian Pædiatric Association. He hoped that it would be published later in a less tentative fashion and in more detail.

M. L. POWELL (Melbourne) thought that they might ask Professor Dods whether tonsillectomy had any influence in preventing recurrence.

S. WILLIAMS (Melbourne) assured the speakers that they had no need to be modest or to be anxious about what they had had to relate. He had been greatly helped by their summaries and impressed by their information. Possibly very few people there realized that a little touch of Boston left Harvard and had graced Australia for many years, and that Professor Ward had not recently taken an interest in the hæmolytic streptococcus, but had been a world authority for many years. The few sentences he had passed on—with due modesty and with the restriction that he lacked his fifty yards pitch to pace up and down—were the gleanings of the middle third of a brilliant life, and Dr. Williams hoped that from the next third the fuller answer would be produced.

D. C. JACKSON (Brisbane) spoke about the incidence of juvenile rheumatism in Queensland. For some time they had been interested in that aspect, believing it to be much higher than was generally supposed. Since the introduction of notification, the very high number of notified cases had borne out that impression. Dr. Dowd had told Dr. Jackson that the acceptability of diagnosis in those notifications was very high. In the previous year (1954) they had had their final year medical students examining public hospital statistics in regard to admission for various diseases in the hope that it would interest them in seeing the incidence of various diseases in the juvenile community. They had been surprised to find that the incidence of rheumatism was highest at the two ends of the year and there was a distinct dip in the winter—not at all what was expected. As a result of that, Dr. Jackson thought that a study of the public hospital figures which were available for the whole of Queensland might be a useful method of obtaining fairly quick information about incidence. The last complete year for which figures were available was 1953. He realized that the figures were open to all sorts of objections with regard to reliability of diagnosis and so on. The figures for 1953 showed no seasonal variation at all. But they did reveal that the total number of cases in the under fifteen years age group for that year was no less than 456, which was surprisingly high for a State in which the incidence of rheumatism was supposed to be low. That represented a rate of 1·2 per thousand children. The other interesting point revealed by the figures was that the highest incidence was in the south-west and the central west where it was sunny and hot and where everybody was supposed to be healthy. The other region of high incidence was in the far north. Those statistical regions had rates of 2·6, 2·5 and 2·1 per thousand children in that age group. Again Dr. Jackson realized how open to criticism were those observations on a relatively small sample and time period. He put them forward as being interesting and because he thought they showed that there were many aspects of the problem of juvenile rheumatism in Queensland still not understood and worthy of further investigation.

PROFESSOR LORIMER DODS (Sydney) said that Dr. Jackson's very interesting statements were based on a form of notification of acute rheumatism established by Dr. Fryberg, Director-General of Health for Queensland. Dr. Fryberg had prepared a detailed *pro forma* which was completed with each notification. The completed forms were forwarded to Professor Dods's department, and Dr. Bryan Dowd, who had reviewed them, considered that approximately 80% of the notifications conformed to the rather severe diagnostic criteria laid down by the American Heart Association and the Medical Research Council of Great Britain.

L. H. HUGHES (Sydney) said that Professor Ward had mentioned that the mortality in rheumatic fever was comparatively small, but the morbidity was great. The child that had been a source of worry over the years was the one who showed minimal signs of the disease and could yet proceed to become a complete cardiac cripple. Dr. Hughes thought that if they did suspect a child of having rheumatism, it was their duty to see that they had regular surveys to try to establish a positive diagnosis and satisfactory treatment at the earliest opportunity. In order to do this a great deal of help might be obtained from clinical measures, but they had to depend a great deal, too, on auxiliary help, such as the determination of the erythrocyte sedimentation rate *et cetera*. He asked Professor Ward whether estimation of antistreptolysin titres was of any practical help in that regard. It had been used extensively

in some parts of the world and was at present being used at the Prince Henry Hospital. There was one other point in regard to Professor Ward's excellent address. Professor Ward seemed rather to stress the idea that penicillin therapy was the prime factor in the treatment of all patients with acute rheumatism. He had mentioned that if they could forestall the possibility of acute rheumatism by diagnosing a *Streptococcus pyogenes* throat infection and then giving penicillin, beneficial effects would follow. That was, of course, undoubtedly the case as far as the control of the streptococcal infection was concerned, but the largest field of therapeutic usefulness as far as the rheumatic process was concerned lay in the proper administration of salicylates or cortisone or both when the acute attack was first suspected or diagnosed.

ROBERT SOUTHBY (Melbourne) said that since rheumatism so often followed tonsillitis, and since recurrence took place after tonsillitis in such a high proportion of children who had had rheumatism, he wished to hear what other clinicians thought about tonsillectomy as a prophylactic measure. In respect to penicillin prophylaxis, Dr. Southby thought that Professor Ward had raised a very big problem in advocating intensive penicillin treatment for acute tonsillitis, for mothers would ask was it necessary for a child to have half a dozen needles every time he became ill. Dr. Southby had seen children who at the age of two or three years had already had 36 or 42 injections.

DOUGLAS GALBRAITH (Melbourne) said that after Dr. Southby's remarks it was important to let a child deal with his milder upper respiratory infections himself so that he would build up immunity. But the point Professor Ward had discussed, and Dr. Southby had commented on, was whether penicillin should be always used for the child with a definite attack of acute tonsillitis with raised temperature. That could present problems. Dr. Galbraith also asked about the influence of climate and temperature on the hæmolytic streptococcus. Was the variation in geographic distribution of the streptococcus due to people being closer together in the colder areas in crowded rooms, or was some other factor present? Not very long ago one of the plastic surgeons in Sydney had told Dr. Galbraith that there was greater prevalence of the streptococcus in the wards in the winter time than in summer.

HOWARD WILLIAMS (Melbourne) asked whether widespread penicillin therapy for clinically diagnosable streptococcal infections in a large urban community reduced the incidence of streptococcal complications such as rheumatic fever or nephritis. In closed communities, such as army camps or a children's home, the prophylactic use of penicillin for all persons would control streptococcal infections and reduce the incidence of both rheumatism and nephritis. It was well known that many children developed rheumatic fever who had no preceding illness or clinical evidence of streptococcal infection and who had often had a previous tonsillectomy. Was there in fact any evidence to show that penicillin therapy widely used in an urban community did reduce the incidence of rheumatic fever? Dr. Williams also asked what was the evidence to show that penicillin therapy given during an attack of rheumatic fever reduced in any way the severity or the likelihood of recurrence of the disease?

Professor Lorimer Dods said that obviously he did not know the answer, but he tried to teach students that the rheumatic child's tonsils should be removed only because the practitioner who knew the child's clinical history and who had carefully observed the child over an adequate period of time was convinced that the tonsils were a source of recurrent and apparently uncontrollable infection, and not merely because the child had suffered a recent attack of acute rheumatism. Under such circumstances, one might argue that removal of the tonsils might possibly diminish the number of recurrent infections of the naso-pharynx and by so doing might possibly diminish the hazard of further episodes of acute rheumatism.

Dr. Arden had asked about the value of penicillin given orally as a form of prophylaxis. The answer to that question was not known. They had been observing a group of rheumatic children who had been given continuous prophylaxis in the form of penicillin—100,000 units three times a day by mouth. There were nearly 60 children in the group who had been receiving this form of continuous penicillin prophylaxis for periods varying from a few months to more than four years, and so far they had not noted any recurrences of acute rheumatism amongst the children. That was to a certain extent a "selected" group, as it had been necessary to choose mothers who were anxious and willing to cooperate and children who lived in the greater Sydney area. Those children had also received early and adequate parenteral penicillin therapy for any real or supposed streptococcal infection.

Dr. Arden had asked about the advisability of suggesting that penicillin for oral administration should be included on the free drug list for rheumatic children. Professor Dods was sure that Dr. Arden would agree that more information about the proven value of oral penicillin prophylaxis would be necessary before this question could be answered.

Professor Dods said that Professor Ward had asked him to say something about the parenteral administration of penicillin during the earliest possible stage of an attack of acute rheumatism. He believed that with the parenteral route sufficient penicillin to maintain an adequate blood level for ten days should be given as early as possible during an attack of acute rheumatism with the object of completely eradicating any real or supposed streptococcal infection. This parenteral penicillin therapy, which should start as soon as the diagnosis was made, represented the beginning of the long-term prophylaxis which Professor Dods considered was an essential for any rheumatic child.

M. L. POWELL (Melbourne) said that his point about the valve *versus* myocarditis story was really the long-term view. Obviously the child could die rapidly with severe myocarditis; but equally Dr. Powell did believe the child could have quite severe myocarditis, and as long as the valve was affected to a minimal degree, could stage what appeared to be a magnificent recovery, with the possible reservation made by Professor Ward that some of those hearts might give trouble in adult life. The insidious case of Dr. Stuckey's was well known. It all depended on what was meant by insidious and subclinical. Dr. Powell had to mention a patient who had been sent to him. The infection was very subclinical to the doctor who sent the patient, but it was shrieking rheumatism as Dr. Powell saw it, with pallor, rapid pulses and an apical triple rhythm. Dr. Powell based the diagnosis in many such cases on the heart itself and the findings there, and he thought that the heart (the only organ they were interested in) would give the show away fairly early. If the patients did the right thing and presented nodules, *erythema marginatum* and a little touch of chorea, of course it was easy, but most times there were simply pallor, abdominal pain, a rapid pulse rate (but one should not be deceived by the occasional slow rate) and something in the heart such as a long apical systolic bruit. That delicate little interval called the *Q-T* corrected for rate was, he found, so microscopic in its dimensions that it was somewhat difficult to assess. The last case in which Dr. Alan Williams performed an autopsy was that of a patient, aged two and a half years, who died with a normal *Q-T* interval. Dr. Powell was glad that someone had mentioned the length of bed rest; he was sure that much of it was too long. The clinical assessment of the case was very important. The sleeping pulse rate, the temperature, and the return of the sedimentation rate to normal were, he thought, good grounds for getting the patients up. After all, the thing that would worry them in the future was not exercise but further streptococcal infection. They should not go swimming in chlorinated pools. That was an important thing.

Was the allergic child more susceptible to rheumatism? Dr. Powell would say "no". He was not aware that there was a definite relation between that form of allergy and rheumatism. In conclusion, Dr. Powell suggested that they should consider the proposition of asking the Commonwealth Serum Laboratories to make a special supply of penicillin for oral use available for controlled series in the hospitals in the Commonwealth.

EDITH CLEMENT (Canberra) wondered whether there was any connexion between rubella and rheumatism. When the British Expeditionary Force was in France in 1939 they had such severe cases with arthralgia and rashes that patients were being sent home as sufferers from rheumatic fever. She herself had experienced severe arthralgia with rubella.

G. G. L. STENING (Sydney) said that penicillin was producing more and more reactions, affecting skin, respiratory tract and other organs. If penicillin was to be used in a widespread manner for acute rheumatism, he thought it was certain that more and more penicillin reactions would occur causing more and more serious effects.

American work had shown that long-acting penicillin—penicillin in combination with other substances—was most likely to cause sensitivity reactions; then in order of frequency of reactions came topical use of penicillin, crystalline penicillin given by injection, and lastly penicillin used orally.

Seeing that it was the injection of a long-acting penicillin that was more likely to cause a reaction, Dr. Stening suggested that if penicillin was to be used prophylactically the oral route was the one to be used.

M. T. COCKBURN (Adelaide) asked whether anyone could help him to understand what particular conditions repre-

sented a recurrence and an exacerbation. In other words, was it a completely new episode or was it an exacerbation of a slowly smouldering process? What was the aim of prophylaxis? Was the aim to prevent a new infection in those children, or was an attempt being made to suppress an old infection that was dormant?

S. W. WILLIAMS (Melbourne) said that there were a number of difficulties in studying penicillin and staphylococcal throat infections. The first was the taking of a swab. In the out-patient department of the Royal Children's Hospital, Melbourne, 22 children thought clinically to have streptococcal infection had been given a long-acting penicillin to see if it cleared the streptococcal infection. Of those, seven yielded a hæmolytic streptococcus, seven a staphylococcus of variable type, and the others no pathogens. It was difficult, therefore, to say clinically whether a child had a streptococcal infection. It was difficult to say so even after a swab was examined by competent people. Dr. Williams's question was: were the broad-spectrum antibiotics as effective as penicillin in children who appeared to have a streptococcal infection?

CLAIR ISBISTER (Sydney) asked, since rheumatism was considered to be an allergy-like reaction, whether it occurred more often in children who had other allergic complaints, and whether those children were more likely to develop sensitivity to penicillin during treatment.

FELIX ARDEN (Brisbane) wished to hear a little more about the relative merits of penicillin and sulphonamide prophylaxis, because if it could be shown that oral administration of penicillin was significantly better, he really did feel that they as an association should take some positive step towards making it more readily available to children. As all knew, the expense of penicillin for oral use was its great drawback, and was great enough to cause people to stop treatment.

F. W. CLEMENTS (Sydney) said that several people had mentioned crowding as a possible factor in determining the incidence of rheumatism. In parallel with Dr. Dowd's study Dr. Clements and his colleagues had been investigating the sociological aspects of the same children, and there was no evidence in the 100 cases of rheumatic fever investigated in Sydney that crowding was a factor.

R. SOUTHBY (Melbourne) said that one thing of interest made clear was that, whereas it had been formerly believed that acute rheumatism with heart involvement was very uncommon in children under five years, Dr. Dowd's figures showed that in his group 40% of the infections were in children under six years. The insidious case was the difficult one. In such cases, which comprised a big proportion of rheumatic children, the child was only vaguely ill for weeks or months, and then while it was being carefully watched, some clear indication of rheumatism appeared. It was in the preceding weeks that damage was done, often while the child was under observation. Dr. Southby was sure it was much safer to regard the suspicious case as being definitely rheumatic, otherwise, with the parents uncertain and undecided, the child was not kept at rest strictly enough and serious crippling might result.

One other aspect of Dr. Powell's remarks was his emphasis of the importance of valvular damage compared to myocardial damage. Dr. Southby had always been under the impression that both valves and myocardium were damaged, and of these the myocardial damage was the more important.

E. STUCKEY (Sydney) wished to hear something about the subclinical case. He saw a lot of children who presented only the minor manifestations and no major manifestations, and the question had to be faced whether the child had rheumatism or not, and if it had whether it should be rested or not. The child might have pyrexia, a moderately raised sedimentation rate and perhaps nothing else, or perhaps some "growing pains". How did one decide whether that child should be treated as seriously ill or not?

JOHN COLEBATCH (Melbourne) said that one of the problems stressed had been the difficulty of diagnosis of mild rheumatic fever. He would like Dr. Dowd to comment on a concept which he (Dr. Colebatch) had formed from clinical experience, that a family history was of great value in diagnosis, a point not mentioned in the British-American survey. Dr. Dowd's figures showed that 60% of his patients had a family history of rheumatic affection, while this occurred in slightly more than one-third of his controls. It would, Dr. Colebatch thought, be true that in many of his (Dr. Dowd's) families there must have been instances of mild rheumatic fever in which the doctor had not satisfied Dr. Dowd's criteria of diagnosis. So that a family history, if gone into with less rigid standards, might have been found in a good many more than 60% of his cases. In many cases the family history as given might be unreliable or there might be so few relatives that a family history was not likely to be helpful. So strong was Dr. Colebatch's impression of the importance of a family history that if the facts were obtainable and they did not include a family history or some rheumatic disorders, he was usually unhappy about a diagnosis of rheumatic fever; and if there was no family history of rheumatic infection, there was usually a history at least of major allergies.

H. G. RISCHBIETH (Adelaide) asked what was considered to be the importance of impetigo as a preceding infection to rheumatism. He had been struck by the number of cases of juvenile rheumatism in which there was a history or evidence of recent preceding impetigo.

L. H. HUGHES (Sydney) said that Dr. Stuckey had raised a very important point. They had all seen children with insidious illness who, they thought, might be suffering from rheumatic fever, and they had always to remember that well-established carditis might present without any previous history or other clinical evidence of rheumatism. If a child had fever, a raised sedimentation rate and an apical systolic murmur, that child should be regarded as having acute rheumatism and be treated accordingly. The subject of subacute rheumatism had always been a very difficult one, and the diagnosis of rheumatic carditis in children might be one of the most difficult in the whole of clinical medicine. The occurrence of an apical diastolic murmur in a child with acute rheumatism was positive evidence that the heart had been involved in the rheumatic process. But the murmur was often preceded for an appreciable time by a normal third heart sound which had not been previously present. When that sound was heard to develop during an attack of acute rheumatism, it was nearly always a forerunner of an apical diastolic murmur, and should be regarded as positive evidence of rheumatic carditis.

H. N. B. WETTENHALL (Melbourne) said that at the risk of widening the discussion even further, he wanted to ask two questions about the treatment of the acute case. One of the problems that arose was the length of bed rest or of restriction of activities. It was his impression that a child was often kept in bed considerably longer than he needed to be. It would be of interest to know what influence bed rest had on recurrences and morbidity. The second question was the timing of steroid therapy. What patients should be given cortisone, and how long should its use be continued?

S. WILLIAMS (Melbourne) thought that rest was overemphasized in acute rheumatism.

D. G. HAMILTON (Sydney) said that in the last four years he had had the opportunity to make very intimate observations on two of his own children who had had rheumatic fever. One thing that had interested and impressed him was that in both of them the onset was a sudden one with carditis from the first day—an upper respiratory infection and carditis present from the beginning. It was possible of course that there had been an insidious carditis which to a doctor-father had been quite inapparent beforehand and was brought to light only by a febrile illness that prompted examination. But he did not think that was the case, because both children had been well before they became febrile. On the question of the length of time that bed rest ought to be continued and the criteria which should be used to determine the advances that could be allowed during convalescence, Dr. Hamilton thought that there was no better sign than the sense and appearance of well-being in a child. When a child looked well and seemed well and had a good colour, then it was time to start making advances in convalescence. But if, having made an advance, one found that the child again became a bit tired, a bit pale, a bit shadowed under the eyes and lost a sense of full health, then one had gone too fast and that child had to be put back to a greater degree of rest than had recently been allowed. On the question of penicillin in the treatment of streptococcal sore throat in any ordinary healthy child or in a rheumatic child, it was very important that someone should declare with authority whether the long-lasting penicillins were really safe and effective. If pædiatricians were to use penicillin, they should do it thoroughly and give treatment for a week at least. This was a very practical question in general practice, because if a child had acute tonsillitis and the doctor went seven times to give an injection of procaine-penicillin each day, he was not going to be invited to come next time a child in the family contracted tonsillitis. Was it effective, therefore, to give one injection of fortified procaine penicillin the first day, see the child much better next day and give an injection of long-lasting penicillin and let that be the end of the story? If those long-lasting penicillin doses were not really effective, then Dr. Hamilton thought that penicillin was an unsatisfactory and indeed

might even be a dangerous drug to use in general practice, where the demands of the public insisted that the doctor should not come many times to treat the ordinary patient with tonsillitis.

A. WILLIAMS (Melbourne) said that he had performed autopsies on 12 children who died from rheumatic heart disease. Their ages ranged from two and a half to twelve years. In the majority the onset of the disease had been insidious. Occasionally it was not possible to find Aschoff bodies in the hearts. Dr. Williams had not seen a case of rheumatic mitral stenosis in a child, and he did not expect to see one. The mitral valve was often incompetent, however. The mitral lesions were sometimes severe, but in the majority of children the valves did not appear sufficiently deformed to cause embarrassment to a healthy myocardium. As Dr. Powell had stated, the valve lesion would, in the patient living to an older age, be the obvious cause of myocardial failure. But in some of the children who had died, the valve lesions were not sufficient to cause cardiac failure, and there had been little structural damage to be seen in the muscle when studied microscopically. Nevertheless, muscle damage caused in a way that was not obvious histologically must have been the cause cardiac failure and death.

PROFESSOR H. K. WARD (Sydney), in reply, said that the great advantage of reading a paper was that one could dodge all the curly ones. The worst of the curly ones were associated with diagnosis, and on those he might reply: "Comfort thyself; what comfort is in me?" Professor Ward did not know that the laboratory could give much help. He had briefly touched on the estimation of antistreptolysin titre and said it was helpful but not diagnostic. He thought it was worth doing, but it was just one of the criteria on which a difficult diagnosis had to be based. He had been a little disappointed by what Dr. Williams said about the one-shot penicillin, for he realized it was not a practical thing to treat streptococcal tonsillitis by numerous injections of penicillin, and he was hopeful that the one-shot penicillin might be the answer. He would suggest to Dr. Williams that he ask his friend Dr. McLorinan to treat a series of patients suffering from scarlet fever with ordinary penicillin and another series with one-shot penicillin. By comparing the two they might get some more definite answers to the question. If it worked, the one-shot penicillin provided a practical answer.

The question of climate was an extremely interesting one. They used to say in America that the incidence of rheumatic fever decreased as one went south. There had been a famous case in which somebody from Boston sent a child down to Florida to recover from rheumatic fever. Down there he had had a recurrence and was immediately sent back to Boston because the doctor in Florida said he had never seen rheumatic fever and did not know how to treat it. That was not borne out by what Dr. Jackson said about Queensland. There was another suggestion: what was necessary about all those problems was more information—what they would like to know about Queensland was the streptococcal background. In New Guinea streptococcal infection of wounds was quite rare, but the same patients when transferred to a clinic in Melbourne, developed a high percentage of streptococcal infections. What one needed to know was how the streptococcal background in North Queensland compared with that in Melbourne. Just before the war, Professor Ward had received some streptococci from Java, and the types were entirely different from the types in Australia. According to the doctor who sent them, all the diseases which in Australia were normally associated with the hæmolytic streptococcus were absent from Java. Another thing Professor Ward wanted to know about Queensland was whether there were pockets of rheumatic fever such as were seen in New South Wales. Surveys had to be made and were very important. There were a number of surveys that needed to be made, but there seemed to be nobody to do them.

Concerning rubella, Professor Ward had heard the same suggestion made before, but he did not think it had any relationship to rheumatic fever. Now he had another suggestion. In a disease like rheumatic fever with a supposed infectious background, he suggested that those who conducted post-mortem examinations should remember that as well as the knife there were the searing iron, the platinum loop and media. The hæmolytic streptococcus was found in children dead of rheumatic fever in heart valves, in the myocardium and in some of the internal glands. Professor Ward's trouble with rheumatic fever was: where was the inciting agent through that long-drawn-out disease? Was the hæmolytic streptococcus present throughout that entire period, tucked away somewhere, and carrying on its nefarious operations? A lot more information was needed about that point. It was said that the disease was an antigen-antibody reaction. Well, where was the antigen all the time? Professor Ward did not think the microscope would give the answer. The problem had to be investigated bacteriologically.

He had often wondered about impetigo as a cause of rheumatic fever, for it was sometimes staphylococcal and sometimes streptococcal.

Concerning Dr. Clements's story about crowding, Professor Ward said that Professor Dods and Dr. Clements might be able to tell them whether the disease was more common in the crowded suburbs than in the outer suburbs. Professor Ward did not know the answer. He always took it for granted, but it might not be true. He did not think that the wide use of penicillin in rheumatic fever was likely to give rise to many penicillin-resistant streptococci. With regard to tonsillectomy, he thought that Glover in England had shown that tonsillectomy did not really have any influence in determining the number of recurrences of rheumatic fever.

BRYAN DOWD (Sydney) agreed with Dr. Stening that reports of penicillin hypersensitivity and penicillin anaphylaxis had lately become more numerous. However, as he had tried to show, recurrences of rheumatic fever were also frequent—too frequent. Those recurrences were most notable in the five years following an initial attack of the disease. That was the period of greatest hazard. Continuous oral prophylaxis by the use of sulphonamide or penicillin would reduce that risk. It was a matter for each physician to decide, on the evidence available, whether in his opinion the prophylactic benefits outweighed the possible anaphylactic risks so far as oral use of penicillin was concerned.

The sulphonamides, as Professor Ward had said, were not indicated as therapeutic agents in the treatment of hæmolytic streptococcal infections. As prophylactic agents, they were not to be despised. The one great theoretical advantage of penicillin over the sulphonamides was the fact that no β-hæmolytic streptococcus (Lancefield Group A) had yet been observed to develop resistance to penicillin in the human body. That, of course, was not true of the sulphonamides. In civilian communities, however, the empirical evidence for the effectiveness of sulphonamide prophylaxis in preventing rheumatic recurrences was very impressive. The sulphonamides also had their disadvantages, but they were effective. Sulphonamide prophylaxis was better than no prophylaxis.

Dr. Dowd thought that most people would now agree that pædiatricians possessed some potent prophylactic weapons against that disease, but prophylaxis was still not well understood nor widely practised. Much of the theory behind the prevention of recurrence, at any rate, should be explained to the parent and perhaps to the child in straightforward terms. Their cooperation should be constantly sought. It was also the responsibility of the physician to ensure continuity of preventive measures. Ideally the patient should continue to attend the same physician or the same clinic. Continuity should extend from day to day and from dose to dose. Could the present administrative systems of supervision bear the weight of continuous prophylaxis?

Finally, concerning the so-called "sub-clinical rheumatism", how commonly did that obscure form of the disease occur? Dr. Dowd knew only too well that rheumatic fever was a much wider entity than the present feeble attempts at classification would imply, yet it was necessary to beware of too frequently using that facile phrase. Had anyone followed a series of patients whom he believed to be suffering from subclinical rheumatic fever over a period of time until the diagnosis became more definite? How common was that occurrence? It was a subject about which all would like advice.

Prevention of Accidental Poisoning in Childhood.

A round table discussion was held on the prevention of accidental poisoning in childhood, F. W. CLEMENTS in the chair.

F. W. CLEMENTS (Sydney) suggested that the meeting should consider the data which would help in the development of a satisfactory programme of prevention of those types of accidents. He said that it was not proposed to consider the treatment of any type of poisoning, except in so far as such matters related to prevention. The data to be presented had been drawn from three sources: (*a*) the sociological study by Miss Jean Allen into the background of some 450 children who were treated at the Royal Children's Hospital, Melbourne, for accidental poisoning; (*b*) the study of some aspects of the history of children treated at the Royal Alexandra Hospital for Children, Sydney, by Dr. J. Beveridge; (*c*) the results of a retrospective study made by himself into the history of accidents during the pre-

school period of life of some 23,000 children drawn from all States of Australia, the majority of whom, however, came from New South Wales.

The session would be divided into three parts: Part I, "The Extent and Nature of the Problem"; Part II (*a*) "Why Children Take Poisons", (*b*) "What Happens when Children Take Poisons"; Part III, "Prevention of Accidental Poisoning".

Part I.

F. W. CLEMENTS (Sydney) read a paper entitled "Accidental Poisoning in Childhood: The Extent and Nature of the Problem" (see page 211).

Part II.

The chairman invited MISS JEAN ALLEN, a guest of the Association, who is the medical social worker at the Clinical Research Unit, the Royal Children's Hospital, Melbourne, to present certain aspects of her sociological study (see page 213).

JOHN BEVERIDGE (Sydney), one of the guests, read a paper on "What Happens when Children Take Poisons" (see page 216).

JOHN WILLIAMS (Melbourne) commented on Miss Allen's observation that the children who had taken poisons seemed to be particularly lively and relatively more advanced for their age, in that they quickly put into their mouths the noxious substances in their reach, and asked whether such behaviour was not consistent with the characteristics of normal development. He pointed out that it was extremely difficult for mothers to keep children out of mischief, and that a considerable degree of protection from potential poisons was necessary.

Miss Allen replied that, although she recognized that it was the normal behaviour for infants and young children to place things in their mouths, it seemed to her that the majority of children in her study had been particularly quick to do this as soon as they had access to the poisonous substances.

F. ARDEN (Brisbane) pointed out that many pharmacists dispensed pills, tablets and capsules in cardboard containers which were easily opened by infants and young children. He suggested that as a precautionary measure all pills and tablets likely to be toxic to children should be dispensed in screw-top jars which could be fastened securely so that the child would have great difficulty in opening them.

Miss Allen stated that the majority of the tablets and pills were in easily opened containers, but that another characteristic of the study was that many of the children had searched in drawers and found a container of tablets which the mother had thought she had securely secreted; she gave as an example a ten months old infant who leaned out of its cot, opened a drawer, searched beneath the contents and even beneath the paper in the bottom of the drawer, and removed a container containing barbiturates, some of which it swallowed.

R. SOUTHBY (Melbourne) asked why so many two to three year olds drank kerosene.

L. P. WAIT (Melbourne) asked if it was because children were unduly thirsty, and inquired if there was a higher incidence of children who drank poisons in the summer time.

Miss Allen said more liquid substances like kerosene were drunk in the hot weather.

M. COCKBURN (Adelaide) asked how much actual fluid was consumed when a child drank a substance like kerosene.

Dr. Beveridge, in reply to Dr. Cockburn, said that in his opinion a minimal amount of substances like kerosene was consumed; a good deal was spilt on the child's clothes, which gave a strong smell of kerosene to the child.

V. COLLINS (Melbourne) asked Miss Allen what percentage of children who swallowed pills or tablets accidentally did so because they were similar to something that the child liked, or because they had a pleasant taste. Dr. Collins also asked whether someone could explain why there had been 419 cases of acute poisoning treated at the Royal Children's Hospital, Melbourne, and only 59 in the Royal Alexandra Hospital, Sydney.

Miss Allen, replying to Dr. Collins, said that many of the tablets were sugar-coated or had other enticing flavours.

Dr. Beveridge, in reply to Dr. Collins's second question, pointed out that whereas the Royal Children's Hospital, Melbourne, served the whole of Melbourne in respect of accidents, including poisoning, the Royal Alexandra Hospital, Sydney, acted purely as a district hospital for accidents. All other metropolitan and suburban hospitals were used for the treatment of emergencies in children.

Part III: Prevention.

S. BELLMAINE (Sydney) thought that more use should be made of the radio in health education campaigns, and particularly in campaigns of accident prevention, including the prevention of accidental poisonings. He would like to see a Children's Safety Council established, which would give advice over the radio to parents on safety procedures. He pointed out that that could be conducted by the Department of Health, as it would seem that Government departments, for example the Department of Railways, was engaged in direct advertising. Such a campaign must be intensive and relate to specific problems.

HOWARD WILLIAMS (Melbourne) said that when this social study of accidental poisoning was originally planned, it was thought that adverse social conditions and poor maternal care would be responsible for a considerable number, if not the majority, of the accidents. The results had turned out quite differently. Approximately three-quarters of the children came from good homes; the mothers were careful and conscientious, and the fathers belonged to the professional, business or skilled tradesmen class. Negligence, carelessness and poor social circumstances were not major factors in the community pattern of poisoning.

The problem was a large one, as approximately one in every 130 children in the age group one to three years took a poison. What, then, were the important factors responsible for poisoning being so common, especially in the economically and socially favourable groups of the community? Dr. Williams said that three important factors emerged from the study. First, many children appeared to be very active, alert and inquisitive and seemed to be different from their fellows. Second, almost half of the poisonous substances swallowed were readily accessible to the child. Third, the mothers did not realize that over one-quarter of the substances were actually poisonous.

Prevention should be possible in many cases with appropriate education, especially as the socially and economically more favoured groups were more commonly involved. Accident prevention, of which poisoning was one important aspect, should be taught to mothers. This was probably best done on the New Zealand pattern; there welfare nurses received special training and paid regular visits to homes to give instruction personally to mothers. Mothers' clubs, kindergartens and other similar organizations could all help by suitable demonstrations and talks. Wireless and newspaper propaganda could help in a limited way, but real education could be learnt only in the home.

Finally, Dr. Williams said he considered that the Australian Pædiatric Association should continue research work on different aspects of accident prevention, as accidents now assumed so large a part in mortality and morbidity rates in healthy children. The Association should be a driving force to inquire into and help prevent accidents, and he would like to move formally that a subcommittee be set up to further that end.

M. B. MEREDITH (Melbourne) thought there ought to be a much more positive approach in advice to parents. The idea that education should be of a negative character advising parents not to do something should be replaced with a positive programme advocating that parents should provide suitable play equipment so that the child would not get into undue mischief.

R. Southby supported Dr. Bellmaine. He felt that programmes should be more intensive and that the Australian Pædiatric Association should be prepared to advise the health departments about active educational campaigns designed towards the reduction of accidents, and particularly accidental poisoning. He thought that the incoming executive should consider the establishment of a committee within the Association on the prevention of accidents.

S. E. J. ROBERTSON (Sydney) said that a certain amount of protection of children from accident hazards and from access to poisonous substances was necessary, and that that should be supplemented with attention directed towards acquainting the child with the hazards of various types of accident situations. He thought children should be discouraged from taking unknown liquids and tablets by giving them an experience with a harmless but nauseous preparation.

Dr. Clements, from the chair, thanked the principal speakers and those who had taken part in the discussion. He thought the main points brought out in the papers and discussion could be summarized in the following way:

1. Accidents, of which accidental poisoning was one type, were by far the most serious cause of death in childhood in Australia, and yet relatively little had been done by the community.

2. Miss Allen's study had clearly shown the need for similar studies in respect of other types of accidents, for her investigation had demonstrated that many commonly held beliefs about how and why children had taken poisons were wrong.

3. Although it would seem from Miss Allen's study that it was the very active, alert and inquisitive child who swallowed poisons when he found them, there was some doubt whether that was not just an expression of a phase of normal development, and whether action of that kind might reasonably be expected of any child. The important thing might be for parents to endeavour to see that all noxious substances were "out of reach" of children always.

4. Dr. Beveridge had demonstrated that certain substances were very dangerous as potential poisons for children, for their significance was frequently not recognized by either doctors or parents; of particular importance were weedicides and pesticides, and drugs like ferrous sulphate, digitalis, "Benzedrine" and the antihistamines, which could cause serious and fatal illness.

5. Prevention was a matter of protection of infants and young children, and of education of older children. That responsibility finally rested with parents, who should, however, be helped with techniques and advice by all available media. The radio could play a prominent role, but guidance on a personal basis, such as might be given by general practitioners and nurses, might be more valuable. The main problem was to keep doctors and nurses fully appraised of the problem.

6. The establishment of a Poison Information Bureau in association with a large metropolitan hospital in each capital city could help in solving many immediate practical problems for practitioners, and in providing a general poisons educational service.

Diabetes Mellitus in Childhood.

S. E. J. ROBERTSON (Sydney) read a paper entitled "Some Aspects of Diabetes Mellitus in Childhood" (see page 218).

ELIZABETH TURNER (Melbourne) said that the number of children Dr. Robertson had described as attending the clinic of the Royal Alexandra Hospital for Children in Sydney was remarkably small as compared with the number attending the Royal Children's Hospital, Melbourne. Did they represent only a section of the community?

F. ARDEN (Brisbane) asked Dr. Robertson if he had had any experience with unrestricted diets. They had changed over to them in Brisbane some years previously and had felt very satisfied with the results. They allowed the mother to vary the insulin dose at her discretion and had found considerable improvement in the emotional well-being of the child with, if anything, a diminished complication rate.

DOUGLAS GALBRAITH (Melbourne) was interested in Dr. Robertson's cases of diabetes associated with epilepsy. He had seen a similar combination, the epilepsy starting after the diabetes had been discovered and treatment with insulin commenced. There was unusually considerable variation in the blood sugar content. The blood sugar level dropped before the fit, and after the fit there was a marked increase.

M. COCKBURN (Adelaide) remarked that when Dr. Robertson said he had no difficulty in getting a child to empty its bladder and then pass urine again in half an hour, he wondered if Dr. Robertson had some trick to help a child undergoing that regime. Dr. Cockburn did not find it easy to get a child to urinate every half an hour.

D. JACKSON (Brisbane) asked Dr. Robertson what insulin policy he recommended for children with proved diabetes but with intermittent or occasional glycosuria. Should those children have insulin, and, if so, how much?

HOWARD WILLIAMS (Melbourne) said that the disturbed water and electrolyte metabolism in diabetic coma was one of cellular and extracellular water loss, a low pH, low carbon dioxide combining power in the extracellular fluid, and often a hyperelectrolytæmia. In the treatment recommended by Dr. Robertson he used physiological or isotonic sodium chloride solution, with added molar lactate and potassium chloride. Would he explain why he used a hypertonic solution with potassium before renal function was established?

Dr. Robertson, in reply to Dr. Turner, said that there were not many children in the diabetic clinics of adult hospitals in Sydney. He did not know why Melbourne should have so many.

The free diet was a very interesting question. Dr. Robertson's private patients were on free diet, but in a hospital with a diet kitchen and dietitians it was so much easier to arrange a strict diet. In private practice free diet was much easier, and his own impression was that it would produce just as good results in the long run. But in hospital practice they had the facilities and they used them and he was hoping to obtain some impression of which group achieved the best results.

Dr. Galbraith was obviously mentioning a very difficult child to control. Dr. Robertson would like to know what insulin the child was having, what its emotional background was and what the home was like before trying to assess what was going on. He would suggest that the severe epileptic phenomena probably followed severe hypoglycæmia.

It sounded difficult, as Dr. Cockburn had said, to get two specimens separated by half an hour. At first it was difficult, but after about three months it was quite automatic and there was no difficulty. It was a matter of persistence and caused trouble only in the first few weeks.

In response to Dr. Jackson, Dr. Robertson said that he felt sure the child's carbohydrate tolerance would decrease and it would need insulin. The things that brought on glycosuria in such a child were increased carbohydrate in the diet, emotional disturbance or infection. After diagnosis, a child could often be controlled for three to six months on diet alone, but after that he required insulin and required it forever. He quite agreed with Dr. Williams that in diabetic coma there was hyperelectrolytæmia and ketosis. They added molar sodium bicarbonate and potassium, one milliequivalent to the cubic centimetre, in their initial infusion, and that would make a hypertonic solution. However, they did not think it had done any harm. Every child in whose treatment they had used potassium had been passing urine. The child diabetic not passing urine was extremely rare.

Syndrome in Infants Resulting from Maternal Emotional Tension.

ELIZABETH K. TURNER (Melbourne) read a paper entitled "The Syndrome in the Infant Resulting from Maternal Emotional Tension during Pregnancy" (see page 221).

D. G. HAMILTON (Sydney) congratulated Dr. Turner on her enthusiasm in carrying out her survey. Many pædiatricians for a long time had felt that prenatal emotional tension might influence the fœtus. A good deal more work along that line should be carried out. Two things ought to be kept very clearly in mind in all such surveys. First it had to be remembered that genetic influences would determine the behaviour of the baby after birth just as environmental influences would, and the mother who was suffering excessive emotional tension during pregnancy might well be suffering that tension because of the nature she had inherited and would in turn pass on to her baby. Secondly, investigators should be very careful to realize that the emotional tension which the mother suffered during pregnancy might continue after parturition and so the environment of the neonate might very well be an anxious one, and influence its behaviour. Dr. Hamilton wondered indeed if the importance of environment went right back to conception and whether there were more factors than pure genetic ones in sorting out the chromosomes that went to form the pattern of the fœtus and the subsequent child. Dr. Turner had taken them back to Saint Luke and to the sixth month. Let them go back to one of the old Hebrew patriarchs and to conception itself. In Genesis that cunning fellow had agreed to take as his pay all those animals in his uncle's herd whose skins were striped or spotted. And in the places where the herds came to mate he placed striped rods of poplar and hazel and chestnut. And behold, all the young had stripes. Or to the Irish horseman—and where but in Ireland could one get a really horsey horseman—who would say that if one wanted a foal with a flare on its forehead, all one had to do was to lead a horse with a flare in front of the mare while she was being served.

PROFESSOR LORIMER DODS (Sydney) said that Dr. Hamilton's reference to Jacob and Laban reminded him that Tristram Shandy's lack of concentrating ability was reported to be due to the fact that Mrs. Shandy asked Mr. Shandy at a most unfortunate emotional moment in their life whether he had remembered to wind the clock.

He was interested to learn from Dr. Turner that there were no obvious congenital malformations in her series.

C. WALKER (Sydney) said that the type of infant referred to had been a worry to him for many years. Those hyperactive infants were a great anxiety to parents and doctors. One very rarely saw a child of that type unless the parents had similar difficulties themselves. Almost always the parents were over-anxious and over-emotional. In the babies who vomited right through the first year of life, one would often find that the mother and the grandmother had done likewise.

There was nothing physically wrong with such children. As far as intrauterine activity was concerned, Dr. Walker had kept a note of such cases for many years, and the fœtuses who were very active *in utero* were usually very active, difficult, excitable children afterwards. He did not know how to quieten them. At about nine months he would give as much as six to eight grains of bromide, four grains of chloral and half a grain of phenobarbital, and the mother would say that she gave a double dose and still the baby was awake all night. He asked Dr. Turner what sedation she used.

Dr. Turner, in reply, said that she had mentioned that it had been necessary to consider the constitutional and hereditary factor. What she tried to stress was that prenatal environment was important too. The illegitimate babies for adoption did behave in a different manner, and that had impressed her and had led her to undertake the survey. She agreed that it was very difficult to sedate the over-active child who stayed awake all night.

Undescended Testis.

A. MURRAY CLARKE (Melbourne) read a paper entitled "Undescended Testis: When and Why to Operate" (see page 222).

C. J. H. GIBSON (Sydney) said that until recently he had been of the opinion that one should operate for undescended testis when the patient was about eight or ten years of age, hoping that before then the testis might descend spontaneously. The assessment of results did not give much hope for a good functional result; a good anatomical result was common—a normal-sized testis with normal sensation lying well in the scrotum. But from a functional point of view, especially that of spermatogenesis, operation did not seem to achieve very much. In 1949, Hansen, using sperm counts as an index of fertility, had followed up a great number of patients with both bilateral and unilateral cryptorchidism, some untreated and some treated. All considered there had been so many sperm counts done on normal individuals that fertility could be assessed by means of the number of sperms, proportion of abnormal forms, and total amount of ejaculate. Hansen's conclusion was that in no case could he say there was a significant increase in fertility as a result of operation. Dr. Clarke had referred to the histological picture. In the last few years a number of studies had been made and it seemed apparent that a great number of undescended testes were inherently abnormal, and that might be the reason why they did not descend. But up to the age of about five or six years, histological studies showed that there was very little difference between the descended and the undescended testis. In the case of unilateral cryptorchidism, biopsy findings from descended and undescended testis were closely parallel to the age of five years. From then on the abnormally situated testis did not develop to the same extent. It lagged more and more behind, and by the prepubertal phase immature seminiferous tubules were apparent and often spermatogonia was absent. So it seemed to Dr. Gibson that in considering the time of operation, if they were to achieve anything from a functional point of view, they should perhaps operate earlier. The degenerative changes, the fibrosis, the tubular regression that occurred did not become very manifest certainly till after puberty. But the question of immaturity, which was distinct, did become apparent soon after the age of five or six years. Thus Dr. Gibson was beginning to wonder whether—granted that the technique of surgery should be gentle, for the structures were very fragile—more might not be achieved by operating on the children before the age of six years. Thus they could give the testicle every chance to develop, assuming that noxious influences associated the malposition might play some part in inhibiting its normal functional development.

A. WILLIAMS (Melbourne) said that in Melbourne they had made a study of the normal and the undescended testis in unilateral cryptorchidism. The appearance of an undescended testis was very like that of a child under five years of age. Compared with the normal, the seminiferous tubules were small, cell differentiation had not occurred and in some there was a slight increase of interstitial tissue. In older boys he had expected to see some degree of fibrosis such as was pictured in Meredith Campbell's book, but that was not present.

J. STEIGRAD (Sydney) said that he had the utmost admiration for any man who dared to elect to discuss undescended testes before a body of experts. Among pædiatric surgeons it was a subject likely to produce argument far more readily than any other. Dr. Clarke had described the retractile testis, the ectopic testis and the partially descended testis, and with this classification Dr. Steigrad agreed as being useful in teaching students, and in assisting in determining treatment. It could be extremely difficult at times to determine whether the condition was one of partial descent or ectopy, and Dr. Clarke had said that he must see the patient more than once to determine this. Dr. Steigrad found it quite difficult sometimes, even at operation, to decide if the testis was imperfectly descended in its normal line of descent or was ectopic in position. He referred to his own attitude to the use of gonadotropic hormone. In 1933 and for a few years he had treated 42 patients with this hormone, but could not really convince himself that the injection of the substance ever brought down a testis that would not have descended of its own accord. He still felt the same way about it and wondered if cures by the hormone were not restricted to the retractile testis which in fact did not need treatment. One question had not been answered. Did anyone have real proof that bilateral orchidopexy had produced a man who had, in fact, produced children? He had kept records of a series of these and had sent out a *questionnaire*. He found two patients who had bilateral orchidopexy and who had one and two children respectively.

Professor Dods asked whether Dr. Clarke would make any comments on testicular "sensitivity", its explanation and its significance. Professor Dods had assumed that the development of "sensitivity" proceeded *pari passu* with the growth of the testis, but recently he had begun to doubt this assumption, as, during pubescence, large, well-developed testes might be relatively insensitive, while small apparently immature testes might be obviously "sensitive".

Dr. Clarke said in reply to Dr. Steigrad that he had seen two people who had been operated on for bilateral undescended testes, and they each had two children. He still thought that if a person had bilateral impalpable testes, there was a definite indication for surgery from the psychological point of view alone. If only a good anatomical result was required, one would wait until the patient was fairly old, otherwise atrophy after early surgery might leave him with virtually nothing in the scrotum. Such a wait might sacrifice a few testes from a functional point of view (and there was no guarantee that they would have been any good anyway), but it might allow the testis in some doubtful cases to descend spontaneously.

Childhood Schizophrenia.

JOHN F. WILLIAMS (Melbourne) read a paper entitled "Childhood Schizophrenia" (see page 224).

W. S. RICKARDS (Melbourne), after expressing appreciation of the full and comprehensive picture of schizophrenia in childhood given by Dr. Williams, made some observations based on data that were agreed upon by a variety of workers. The outstanding feature of the literature was that workers working from such widely separated viewpoints as psychoanalytical theory and practice to genetic theories and biochemical theories somehow just did not seem to get together. But from all the work there seemed to emerge the fact that this was an abnormal reaction of presumably a predisposed child to a particular emotional environment. Many syndromes which fell into the group of schizophrenia had been described. They had been described because the varying factors such as the intelligence of the child or the nature of the symptoms he displayed seemed to fit a rather striking clinical picture. *Dementia præcox* and infantile autism, given certain circumstances, did present a rather characteristic picture. But in clinical practice there were very many grades that did not fit the syndrome as described. For that reason different workers used very different criteria of diagnosis. The Maudsley Hospital was conducting a very wide investigation of this kind. They had many workers of many disciplines who were studying those children objectively for a period of time. As a result, some surprising facts were being revealed. The first child had a positive Wassermann reaction. The second was hydrocephalic. The third had the grossest emotional trauma one could imagine. It was well known that electroencephalographic abnormalities were common. A tremendous amount of adult schizophrenia had been shown to be related to endocrine changes. That contrasted with the great bulk of the literature which was a psychoanalytical study of the child and his emotional relationships with his environment.

Dr. Rickards remembered one child, who was grossly out of emotional contrast with his environment and who was treated in a completely impersonal way. From the point of view of perception, visual and motor coordination, drawing, *et cetera*, he was simply brilliant, and even on intelligence tests, devised for normal children and so involving speech and educational problems, he gave an intelligence quotient of 125, mute as he was. The big problem with him was

deafness. At the children's hospital they had found that it was very useful to have in the team a psychiatrist, a psychologist, a play therapist, an audiometrist and at times a speech therapist. That team approach was very important. They had seen deaf children develop a schizophrenic picture. True mental defectives could also give the picture of schizophrenia.

Dr. Williams had mentioned psychotherapeutic treatment. The treatment was essentially psychotherapy by competently trained people. With a properly orientated approach, the results were perhaps not quite so prognostically bad. In Boston where child, mother and father were taken and treated intensively over a period of time, of 65 patients only six had had to be admitted to institutional care. It seemed that the process was reversible. One was often faced with the question of insulin and electroconvulsive therapy. It was doubtful if electroconvulsive therapy did any good to an already disturbed child. Insulin in the prepubertal age group caused considerable improvement, but there was considerable doubt if physical treatments were very much help to the child. In Melbourne there were no adequate facilities for the treatment of emotionally disturbed children. They could be sent to mentally defectives colonies or admitted for a time to the children's hospital. When the child was withdrawn and losing affective relationship, at what point was he schizophrenic? It was an urgent problem to provide more facilities for his treatment.

S. E. J. ROBERTSON (Sydney) asked whether the children under discussion ever presented somatic symptoms and appeared to be suffering from an organic illness.

S. E. L. STENING (Sydney) said that he found it very difficult to decide where a behaviour problem ended and where schizophrenia began. One saw many severe behaviour problems in children who seemed to be treatable for a while. Dr. Stening asked whether he would be right in expecting a proportion of these to develop schizophrenia later on. If such children were diagnosed as having schizophrenia, and if treatment was given, was there any chance of permanent cure?

Dr. Williams, in reply to Dr. Robertson, said that the differential diagnosis of schizophrenia was often one of considerable difficulty, and such problems as deafness and cerebral damage were sometimes quite difficult to exclude.

In reply to Dr. Stening, Dr. Williams said that the development of schizophrenia appeared to him to be in many ways quite unique as a behaviour problem, though there were often difficulties of behaviour presenting in the previous history. The important point for diagnosis and treatment was to recognize a tendency to withdrawal and loss of affective relationships before the child became definitely schizophrenic, for, at the former stage, treatment had far more chance of being effective than when the condition became marked; though even then prolonged treatment did give some hope of amelioration and cure.

The Diagnosis of Hæmorrhagic States in Childhood.

JOHN COLEBATCH (Melbourne) on behalf of himself and Betty M. Wilson presented a paper entitled "The Diagnosis of Hæmorrhagic States in Childhood" (see page 226).

PROFESSOR LORIMER DODS (Sydney) commented on two points. The prothrombin consumption test which they had all found of such value had occasionally failed in the investigation of minor coagulation defects, and Dr. Margolis, who was working in Professor Dods's laboratory, had helped them a great deal by the use of the "thromboplastin generation" test. Professor Dods did not want to suggest for a moment that a complicated test of such a type should be applied to all coagulation disorders, but he was convinced that it was of help in sorting out some of the more difficult problems and was a protection from the occasional deficiency of the prothrombin consumption test. He made a special plea for a simplification of the present nomenclature. Modifications of the word "hæmophilia" should be avoided, as also should a baptism of proper names which might lead to even more confusion. He suggested that, when possible, they should talk about each coagulation disorder in terms of a known deficiency factor, and so speak of coagulation defects due to a deficiency of this or that factor.

Dr. Colebatch replied that nomenclature was very important and was causing confusion everywhere. He agreed that they should avoid using persons' names. If they could accept Professor Dods's suggestion, it would help, but it was not always possible because even the known missing factors had not satisfactory names. This was shown plainly by the prothromboplastin deficiency factors called by different people AHF, PTC, PTA, PTF-D.

Funnel Chest.

RUSSELL HOWARD (Melbourne) read a paper entitled "Funnel Chest". An extended version of this paper was published in THE MEDICAL JOURNAL OF AUSTRALIA of December 31, 1955. He defined funnel chest as a condition in which the normal prominence of the sternum was replaced by a cavity which centred on the sterno-xiphisternal junction and constituted the "funnel". The exact mechanism of production was uncertain. It had been suggested that a short central tendon of the diaphragm pulled the xiphisternum backwards to produce the deformity. That was difficult to harmonize with certain aspects of the malformation, but it nevertheless appeared that the diaphragm had a very large influence in its development, although the influence might be secondary. The other ætiological factor of significance was that a family history of the condition was usually obtainable, and that further deformities of the thoracic cage, such as pigeon breast, might occur in other members of the same family.

The condition was usually (probably always) noticeable at birth. In the infant with a very malleable chest wall a most noticeable feature was that gross retraction occurred on inspiration. As the child grew older the chest wall became more set, and retraction diminished until, about the age of four years, that feature had to a considerable extent disappeared. The usual history given was that deformity was progressive.

The concavity was usually symmetrically arranged about the mid-line and was formed by the dipping backwards of costal cartilages, generally the third to eighth on either side, to meet their sternal attachments. At times an asymmetrical element was present. The upper part of the chest was usually shallow, and poor posture with drooping shoulders, dorsal kyphosis and pot belly was frequently a marked feature. All grades of sternal depression occurred, from the very mild to the very severe.

Apart from the actual deformity, the clinical features might be considered under three headings—respiratory, cardiac and psychological.

Limitation of effort might be marked and was probably referable to diminution of vital capacity. Not infrequently it was disguised by the fact that the child would not attempt exercise which he had learnt he was unable to perform. Post-operatively, one so frequently heard the comment that the child would now do so many things that previously he had not attempted. Minor coughs, colds and asthma were of common occurrence.

There was probably some cardiac element in the limitation of effort, and this might reach a maximum in cases in which gross congestive cardiac failure developed at an early age (perhaps late teens or early twenties). It appeared that this was due to constriction of the heart between the sternum and the vertebral column.

Psychological changes were the rule in all except mild cases. The patient might attempt to conceal them, but they tended to be present and to be progressive. Gibes from school mates frequently started the train of symptoms.

An X-ray examination of the chest would reveal any cardiac displacement (if present, it was usually to the left), and a lateral film demonstrated the degree of sternal depression. A lateral tomogram taken with a centimetre scale placed flat along the mid-sternum gave a completely accurate measurement of this important distance.

Funnel chest could not be cured by any form of physiotherapy or by the wearing of a retentive apparatus.

Dr. Howard described the operation and said that convalescence from the procedure was rapid, the child being up and about on the second post-operative day, and leaving hospital on the tenth. Breathing exercises were most important in this early stage and were continued for a period of approximately six weeks. The age of election for operation was considered to be approximately four years. The governing factor was inspiratory chest retraction, and at this age it had virtually vanished. It had been thought that the minor procedure of simple division of the xiphisternum from the sternum could effect a cure in infants under the age of twelve months. In his series of 40 operative cases the separation had been attempted in six, but the results had been unsatisfactory and the procedure was not recommended. Patients older than the age of election might be operated on at convenience or, should urgent features supervene (congestive cardiac failure), as a matter of comparative emergency. There was probably no upper age limit (certainly not for emergency cases), but the best results were likely to be obtained in children under the age of twelve years.

All cases of funnel chest did not merit operation. The minor grades of the deformity showing no clinical features except slight sternal depression were probably better left alone. About 75% of the patients referred to him were in the operative category.

It was important to emphasize that the poor posture exhibited by so many patients with funnel chest was not cured by operation, and would need assiduous parental care assisted by the help of a trained physiotherapist.

T. Y. NELSON (Sydney) regarded the treatment as anything but a minor procedure. The majority of the cases he had seen fell into the category in which he included 25%. In other words, he did not think they justified operation. This was an important aspect of the question to be discussed by the meeting, for it was a responsibility of the pædiatrician to assess really what symptoms the condition did produce. Dr. Nelson did not think that was at all clear. He was not fully persuaded that it produced gross cardiac irregularities or respiratory difficulties. He thought it was mainly a cosmetic operation, and for that reason should be regarded with a certain amount of reserve.

HOWARD WILLIAMS (Melbourne) said that Dr. Howard had stated that the ætiology of funnel chest in the majority of patients was an inherited defect. It was well to remember that it often occurred whenever chronic respiratory obstruction was present either in the larynx or in the peripheral bronchial tree. Infants with so-called congenital laryngeal stridor due to a laryngeal web, an infantile larynx or other causes might develop a funnel deformity of the chest which would spontaneously resolve in the majority as the respiratory obstruction was relieved. General bronchiolar obstruction as commonly occurred in chronic asthma, or infective bronchiolitis and bronchiectasis might result in varying grades of the deformity. With treatment of the disorder itself and by the institution of physiotherapy, correction was possible. Dr. Williams said that he agreed entirely with Dr. Nelson, who had said that any child with chronic respiratory symptoms and a funnel chest should be assessed very carefully before advising surgical correction of the deformity. Would Dr. Howard tell the meeting how many of the children he operated on had a history of chronic respiratory disease?

E. STUCKEY (Sydney) thought that there was a major and a minor form of the disease, and that the minor form was often associated with respiratory obstruction. He pointed out that in the film he showed the child had marked micrognathism which was liable to produce chronic respiratory obstruction. On the other hand Dr. Stuckey was quite convinced that marked deformity was well treated surgically, and in the cases in which he had operated he had been well pleased with the results.

J. F. WILLIAMS (Melbourne) said that these children certainly became unduly self-conscious about their deformity and there was no doubt that it was a psychological handicap.

J. STEIGRAD (Sydney) said that it was quite obvious from Dr. Howard's paper that he had had far greater experience of the condition than anyone else in the country. Dr. Steigrad had seen eight or nine patients for whom he recommended the operation, but in only two cases was the operation performed. This was so because of the difficulty in persuading the referring doctor that such a procedure was wise.

As far as symptoms were concerned, none of his patients had been referred for anything other than the cosmetic effect. In the two patients operated on, the results had been quite good and the parents had remarked on the fact that the child had become more active since the operation.

Dr. Howard, in reply, said that blood transfusion was always given. Blood loss was measured. The children lost eight to 16 ounces and this was replaced as lost.

Symptoms were very often concealed, and, as Dr. Steigrad had pointed out, parents often said that they thought the child was quite well except for the hole in the chest, but they were surprised how much better he was after operation—how much more readily he ran around, how he could now climb a hill he would never attempt before, and how he now played football which before they thought he did not want to play, not realizing that it was because he could not play. That was the same story as one heard from the parents of children who had been operated on for patent *ductus arteriosus*. The parents had been content with the child's estimate of his own normal beforehand, and they realized after operation that the estimate had been incorrect. Dr. Howard had had one child only with associated congenital laryngeal stridor. He operated on that child at the age of twelve months, and operation would probably have to be repeated. The question whether congenital laryngeal stridor was responsible for funnel chest had been discussed a great deal in America, and the usual opinion was that it was not. He had operated on several children who had had asthma, at first rather unwillingly. Since operation, three of these had had no further asthmatic attacks, so that he was now not unwilling to operate in such cases.

The upper age limit was not fixed. Any patient with cardiac failure should be operated on. The mother, aged thirty-five years, of one of his child patients with funnel chest had a bad funnel chest herself and congestive cardiac failure. Dr. Howard thought she should be operated on, for there appeared to be no other cause for her cardiac failure. Short of cardiac failure, he thought there was not much point in operating on these people above the age of twenty years. Any psychological symptoms would be well ingrained by that time. Once he was sure operation was indicated he liked to operate as soon as possible after the age of four years. Patients about whom there was doubt should be observed until the position became clear.

Progressive Bronchiectasis.

HOWARD WILLIAMS (Melbourne) in a paper on progressive bronchiectasis said that a clinician who critically studied a number of patients with bronchiectasis could not fail to be impressed by the variable pattern and course of the disease in different patients. Evidence collected was strongly against the common clinical and pathological concept that the differences were variants of the one disease process. Over the past seven years he and Dr. O'Reilly had been studying the evolution of the disease from its earliest inception in a wide variety of patients, and it was now clear that bronchiectasis was merely the end result of a number of different disease processes. At two previous meetings two distinct types of bronchiectasis, each with its own pathology and clinical features, had been demonstrated. Those two types were, first, bronchiectasis consequent on collapse and/or consolidation of a segment or lobe due to the invasion of a bronchus by tuberculous hilar glands, and second, that resulting from collapse of a lobe due to pyogenic infection.

The purpose of his paper was to present another equally distinctive type, of which 29 cases had been studied.

Clinical Features.

The disorder almost invariably commenced in infancy, girls being affected approximately twice as commonly as boys. Symptoms commenced insidiously with cough and nasal discharge, which were initiated in the majority of patients by a coryza or bronchitis and in the remainder by pink disease, morbilli or pneumonia. Symptoms of cough and nasal discharge were persistent with exacerbations precipitated by fresh respiratory tract infections. All the children were also subject to sudden attacks of fever and malaise which usually lasted for two to five days. Those attacks were apparently not due to an extrinsic infection. In three-fifths of the patients, wheezing was noted, particularly during the early years and during exacerbations. Constitutionally the child was usually below par in general health. Sputum was not expectorated as it was swallowed and seen only by the mother in vomitus or in the mouth after coughing. Sputum was produced only when the child had been taught to expectorate. The cough, nasal discharge and febrile attacks persisted with frequent exacerbations until later childhood, when they were less pronounced.

Examination revealed patients in poor general health and with poor muscle tone and posture. Respiration was frequently upper thoracic in type, and a kyphosis and bilateral Harrison's sulcus were common. In the earliest stages crepitations were audible over the lower lobes, right middle lobe and lingula, and in some patients rhonchi were also heard. The widespread distribution of the crepitations indicated pulmonary or bronchiolar involvement much greater than was seen in plain radiographs or bronchograms.

Radiographic Changes.

Early radiographs usually showed no other changes than an increase in the broncho-vascular markings, especially in the lower lobes. Later, evidence of parenchymatous involvement was shown by very heavy streaky blurring along the broncho-vascular markings. In some cases mottling was observed and in others an opacity of a segment, especially the lingula and right middle lobe. Bronchograms in children under three years of age usually showed defective fine bronchiolar branching of patchy distribution. Sometimes one or several of the bronchi in a segment did not fill, and the bronchi had a "stumped" appearance with minimal or no dilatation. After several years, further patchy destruction of the peripheral bronchial tree was evident. In some segments fine branching had disappeared and the bronchi

were seen as dilated stumps; in some segments changes were minimal, while in others intermediate changes were present. The lingula and left lower lobe usually showed changes first, but when the disease was fully developed it was uncommon not to have both lower lobes, lingula and right middle lobe affected. In a number of patients the lingula and right middle lobe were collapsed, but collapse was uncommon in the lower lobes.

As far as could be determined, the disease progressed most in the first three to six years, but in a small number further changes occurred in the period from six to twelve years of age. In the period about puberty the lesions often seemed to become stationary and the symptoms of cough, sputum and rhinorrhœa less.

Pathology.

Dr. Williams said that the pathological changes were most probably due to chronic infective bronchiolitis and interstitial pneumonia together with chronic sinusitis. Those infective changes persisted often with exacerbations and produced patchy destruction of much of the peripheral bronchial tree. Many of the alveolar air sacs remained inflated, as they had connexion with other parts of the bronchial tree through the pores of Kohn. The bronchi above the damaged, fibrosed bronchi and bronchioles were partly dilated. The changes usually seemed to be most extensive in the left lower lobe and lingula, but the right lower lobe and/or right middle lobe seldom escaped. The evidence for the changes was first clinical. The clinical signs developed very early, usually before any radiological or bronchographic evidence of disease. The signs consisted of fine crepitations over both lower lobes, lingula and right middle lobe. Frequent exacerbations of unexplained fever and malaise indicated a persistent infection.

Pathological studies had been made by three methods: first, injection of a plastic into the bronchial tree to make a cast, second, serial histological sections, and third, dissection of diseased bronchi to the periphery of a lobe combined with suitable histological sections. The investigations all led to the conclusion that an infective process in the peripheral bronchial tree was the basic pathological lesion. The neoprene casts showed a distorted bronchial tree with much defective or absent branching of the peripheral bronchi and bronchioles. Those that were not obliterated were often dilated and showed irregular narrowing in some areas. Serial histological sections showed varying stages of infective bronchiolitis and interstitial pneumonia. In the early stages the mucosa and submucosa showed acute inflammatory changes with destruction of the elastic tissue. In the most advanced stages the bronchioles were completely destroyed and replaced by fibrous cords surrounded by interstitial inflammatory changes. Dissection of affected bronchi showed that many branches of a segmental bronchus were occluded and finally the bronchus itself was replaced by a fibrous cord in the middle of air-containing alveoli which had no direct connexion with the bronchial tree.

Dr. Williams said that while the morbid anatomical changes were known, many aspects of the ætiology were not understood. Why did the onset of the disease occur in infancy and affect females more than males? Why were the lower lobes, lingula and right middle lobe affected and why was the left side involved more than the right? Why was the clinical and pathological pattern so similar when the disease was initiated by a variety of different infections? Were poor environmental factors, such as overcrowding and poor feeding, of importance? Was the child constitutionally subject to respiratory tract infection? Did allergy play a role? Elucidation of those questions would be necessary before the disease was understood.

Prevention.

Dr. Williams then said that until more was known about the pathology it was difficult to know whether much could be done to prevent the disorder. It was impossible at present to control respiratory tract infections in infants. Frequently the disorder appeared to be initiated by an ordinary respiratory tract infection. The infection was of a non-specific variety and appeared to smoulder for a number of years. In most cases there was no specific or uniform bacterial flora of the respiratory tract. At times a hæmolytic streptococcus or staphylococcus, *Hæmophilus influenzæ* or *Streptococcus pneumoniæ* was isolated, but probably those were secondary invaders. Control of the infection could be attempted only by empirical use of a series of antibiotics. Long courses over months of small doses of different broad-spectrum antibiotics seemed to offer the most rational approach. Assessment of the results of such treatment was very difficult.

As the disease progressed, the basis of medical treatment was to help to control infection by long courses of the wide-range antibiotics. In addition, physiotherapy and instruction in clearing the bronchial tree by coughing and expectorating did much to improve the general health and abolish the febrile episodes. If such treatment was to be effective, the mother had to be convinced of its importance and to see that the child carried out the treatment. Failure to obtain the mother's support and enthusiasm meant failure of this line of treatment.

Surgery.

Dr. Williams said that it was probable that many of the bad results following lobectomy were due to failure to recognize that this was a distinct type of bronchiectasis and was usually progressive in early childhood and often into later childhood. A lobe might be involved in the early stages of the disease and yet show a normal bronchogram. The stethoscope was a much more important and reliable tool than a radiograph or bronchogram in determining whether a lobe was normal. It was their experience that removal of all bronchographically affected lung had led to development of bronchiectatic changes in other segments which were bronchographically normal. Until one was sure that the disease was arrested—and that required observation over some years—it was unwarranted to carry out surgery. When the disease was arrested, assessment had to be made of how much lung would be left after removal of affected parts. Removal of both lower lobes, lingula and right middle lobe was drastic surgery, but if eradication of all affected lung tissue was the aim, then that was the only possible approach. If the disease was confined to two or three lobes, which was uncommon, the decision was easier.

Discussion.

KATE CAMPBELL (Melbourne) said that few had the opportunity to follow the natural history of the disease as Dr. Williams was doing. In this condition there seemed to be a disturbance of the whole respiratory tract, upper and lower, which might be due to an abnormal type of mucus secreted. Was there any change in viscosity of mucus of the respiratory tract or any evidence of change in stools to suggest that these young children might have had a mild mucoviscidosis?

R. GREEN (Sydney) said that Dr. Williams had talked about upper respiratory tract infection in the children under discussion. They had narrow nostrils and high palate which interfered with nasal airway and helped to produce sinusitis, and they showed signs of past rickets. A useful treatment was to move them from the city area up to the hills in a drier climate. That made a great difference to them, and any child suffering from recurrent bronchitis or bronchopneumonia should be given the benefit of a few months in such a climate.

DONALD VICKERY (Sydney) pointed out the very common nature of the disease and quoted figures from the Royal Alexandra Hospital for Children. They had 205 cases of proven bronchiectasis, and 78 of the children had the initial disease in recurrent bronchitis of infancy. If to these were added 34 children with pink disease with protracted bronchitis, they had 40% of Royal Alexandra Hospital cases in Sydney with no history of an illness characterized by massive collapse of a lobe. All the children belonged to an age group in which bronchi were very small and drainage was deficient, and physiotherapy could not be carried out no matter how carefully the attempt was made.

Not all their cases went on to the dreadful stage described by Dr. Williams, although they did see progressive bronchiectasis. Until the children reached a stage at which their bronchi were a little larger and at which they could cooperate with physiotherapy, it was not possible to arrest the process and the disease would progress. Dr. Vickery ventured to say that the recurrent attacks of pyrexia so common in these children were due mainly to the fact that the bronchi were so small, and physiotherapy could not be carried out successfully; actually the children got recurrent small areas of pneumonitis that could not be demonstrated by an X-ray examination. He had been pleased to hear advocated the prolonged use of chemotherapy in this type of case. Despite some differences of opinion, he personally believed that it reduced the attacks of recurrent pneumonitis.

E. B. SIMS (Adelaide) said that some of the children had been observed in Adelaide to have in addition to their sinusitis and bronchiectasis an associated *keratosis obturans* in the ears. This suggested that the defect in some of them might be a more widespread one, genetically determined, and based on an abnormality of secretion or epithelialization. This had been reported recently in the *Clinical Reports of the Adelaide Children's Hospital*. Dr. Sims wondered what Dr. Williams's experience in this matter had been.

T. Y. NELSON (Sydney) asked Dr. Williams whether he regarded the progress of the disease in this type as inevitably downwards. Dr. Nelson thought that they had seen cases that would fall into the group under discussion that had been reversed and had later shown no signs of bronchiectasis. He thought that in a retrospective examination of bronchograms one could usually detect the areas that were affected, and he suggested that in one of the bronchograms shown by him there was no filling of the right lower lobe and later bronchiectasis in that part. This lack of filling Dr. Nelson thought was an important indication of potential or possible bronchiectasis.

Dr. Williams, in reply, said that Dr. Robertson had asked whether the cough in bronchiectasis was persistent. In his experience it was, but it might be less noticeable in the summer. In reply to Dr. Campbell's question whether there was any change in the mucus secreted by these patients and whether any of the cases could be mild or atypical examples of fibrocystic disease of the pancreas, Dr. Williams said that investigations into the mucous secretion had not been carried out owing to the technical difficulties in obtaining suitable samples of uninfected mucus from the bronchial tree. As far as could be determined there was no relation to fibrocystic disease, and in the few cases in which pancreatic function had been assessed the results were normal. Dr. Green had asked about the influence of adverse social factors in the ætiology. Dr. Williams was unable to answer the question. A planned study of social factors in various types of bronchiectasis was to be commenced later in the year. Dr. Vickery's view on the value of prolonged physiotherapy and chemotherapy was in agreement with experience in Melbourne. Dr. Sims had asked about the incidence of *keratosis obturans*. The condition was present in many patients, but by no means in all of them. Dr. Nelson had commented that one of the X-ray photographs showed non-filling of part of a segment before the development of bronchiectasis, and asked whether that was always so. He had also asked whether the course of the disease was always downhill. In some patients there was evidence of non-filling in portions of segments, the cause being presumably obstruction from inflammatory swelling or secretion or both. However, in others there was no evidence of non-filling in the stage of clinical bronchiolitis, for on auscultation numerous persistent crepitations were heard over the area. The natural history and varying degrees of this type of bronchiectasis were not completely known. Dr. Williams's paper dealt with 29 severe examples, but there were probably many other patients with less severe forms of the disease.

Infectious Lymphocytosis.

DOUGLAS GALBRAITH (Melbourne) read a paper entitled "Infectious Lymphocytosis" (see page 230).

FELIX ARDEN (Brisbane) said that Dr. Galbraith deserved the congratulations of everybody present, not only because he was lucky enough to light on the first two cases, but much more important, because he went out looking for the third case. He was perhaps the first man in medical history who had gone out looking for a patient with acute infectious lymphocytosis and had found one. He deserved congratulations for the "Dr. Pickles-like" way in which he had obtained his results. Dr. Arden knew that he himself might have discovered such a case and considered it interesting and then let it drift away; but Dr. Galbraith had followed it up with great care, and he had contributed greatly to the not very exhaustive literature on the subject. The questions that occurred to Dr. Arden, looking at his slides and hearing about the tendency to lymphoblasts in the film, were whether Dr. Galbraith could tell them a little more about the bone marrow and whether there was any connexion, however tenuous, between the disease and lymphatic leuchæmia.

Dr. Galbraith thanked Dr. Arden, and in reply to his question about the bone marrow, said that biopsy had been carried out on only one child and did not show any definite abnormality. He would be glad to show Dr. Arden a complete report of bone marrow biopsy. He could not comment on the problem of any relationship between infectious lymphocytosis and lymphatic leuchæmia.

KATE CAMPBELL (Melbourne) asked whether the other children in the hospital who developed whooping cough were also having anti-tuberculosis drugs and if anti-tuberculosis drugs might affect the disease.

Dr. Galbraith said that several children who developed whooping cough did not have a tuberculous condition and were not being treated with anti-tuberculosis drugs.

STANLEY WILLIAMS (Melbourne) said that the story rang true to him and it fitted in very neatly and nicely, and he thanked Dr. Galbraith for a lot of useful information. As he had stated, high and low counts in whooping cough were recorded and generally the counts were more in the neighbourhood of 20,000 to 40,000. But as many there probably knew, it was not uncommon that the odd child with cough and anæmia and a high leucocyte count of 80,000 to 100,000 per cubic millimetre was not suspected at all of having whooping cough, but of having leuchæmia.

S. E. J. ROBERTSON (Sydney) asked whether any of the children had developed diarrhœa, and if a search was made for *Giardia lamblia*.

Dr. Galbraith said that he had noted in the literature the question of *Giardia lamblia* producing a blood picture with lymphocytosis and had therefore had stools examined, but with negative results. One of the children had symptoms of mild diarrhœa, but nothing characteristic had been found.

PROFESSOR L. DODS (Sydney) thought that the cases described by Dr. Galbraith conformed in every respect to the clinical and hæmatological picture of acute infectious lymphocytosis. Could Dr. Galbraith please tell them at what stage of whooping cough the anti-hæmagglutinin titre reached a level which was recorded as "positive".

Dr. Galbraith said that he could not give a great deal of information about the question of the anti-hæmagglutinin titre in pertussis. Dr. Stephen Fisher had carried out the tests. Possibly Dr. Stanley Williams could give additional information. The time taken for the result of the test to become positive seemed to vary considerably; although it might be positive within a week or two, the average time seemed to be three or four weeks before the titre became sufficiently high to be diagnostic. In one child studied the test gave a negative result at forty-six days after cough commenced, but the result was positive at one hundred days after cough commenced. In conclusion, Dr. Galbraith said that he had really wished to emphasize the advisability of carrying out routine blood investigation in children under observation in long-stay hospitals, and he thought that if this was conscientiously done, it might be possible to build up a fund of knowledge on the subject.

JOHN COLEBATCH (Melbourne) was sure that Dr. Galbraith was glad to have the reassurance of the several speakers on this subject because there had been some criticism and scepticism in certain circles in Melbourne about it, and Dr. Colebatch thought that Smith had met the same criticism and scepticism when he first presented the syndrome as an entity. The two chief things against the possibility were the presence of blast cells in the blood and, perhaps, the lack of evidence of widespread infectivity of the condition. Dr. Galbraith had mentioned his (Dr. Colebatch's) opinion that the presence of blast cells was due to the combined effects of tuberculosis and infectious lymphocytosis. Tuberculosis, they knew, would disturb the normal marrow reactions, and the occurrence of infectious lymphocytosis in a tuberculous patient was why blast cells turned up. That was his explanation.

Megaureter.

F. DOUGLAS STEPHENS (Melbourne) read a paper entitled "Megaureter" (see page 233).

E. STUCKEY (Sydney) had had personal experience of the value of triple micturition after operative treatment in certain patients. He thought it was a very useful procedure. He did not think it was always quite as easy as Dr. Stephens made out by showing a suitable patient. Dr. Stuckey had some films of a patient who had urethral obstruction, which showed that at the end of triple micturition the ureters were practically as full as they had been before. That, however, was a rare phenomenon, and Dr. Stuckey thought that such a patient might have to pass urine five times. Those cases were a puzzle when one could not find the mechanical reason for the apparent obstruction. He had had no personal experience of converting the cases without reflux into cases with reflux as Dr. Stephens had done.

Dr. Stephens said that he was not very familiar with the degree or efficiency of triple micturition when there had been urethral obstruction. He had not had very many such patients with gross reflux. As Dr. Stuckey said, his patient was one of the group in which the child might have to pass urine five times. In that group with obstruction at the lower end of the ureter Dr. Stephens did find it harder to secure emptying by repetitive micturition, but in the idiopathic reflux group he had rarely found a reasonably cooperative child who had failed to empty the urinary tract completely in three attempts. One did have a problem with the very uncooperative child, especially in the under two years age group.

D. G. HAMILTON (Sydney) asked what difference to the problem the existence of urethral obstruction as the cause of the megaureter made.

Dr. Stephens said that the dilatation of the ureter in the non-reflux group and in the urethral obstruction group was secondary to the obstruction. In the other group it was a primary deformity. He thought that there was more difficulty in emptying the ureter when there had been an obstruction as the basis of the dilatation. Dr. Hamilton then asked whether the ureter came back to normal and if there was difficulty in the emptying of it when the obstruction was urethral, a urethral valve for example, and it was removed entirely.

Dr. Stephens replied that unless it was only very little dilated, it would not come back to normal, though in an excretion pyelogram it did sometimes look normal. It could often be blown up to its old size through a retrograde catheter. It did recover its emptying power. When the obstruction was removed, reflux would gradually stop.

H. N. B. WETTENHALL (Melbourne) asked whether on the analogy of Hirschsprung's disease and the absence of Auerbach's plexus there was any evidence to suggest that obstruction of the lower end of the ureter could result from the absence of nervous tissue at that point.

Dr. Stephens said that he had not discussed ætiology of megaureter because of the shortness of time. The two groups of megaureter, those with reflux and those with obstruction, were often confused. Swenson, of Boston, had demonstrated a partial absence of ganglion cells in some cases of megaureter associated with enlargement of the bladder. He attributed the megaureter to the deficiency in innervation of the bladder. Treatment in this group, he considered, should be directed towards the bladder and bladder neck.

The Wringer Injury.

DAVID L. DEY (Sydney) read a paper entitled "The Wringer Injury" see page 234).

J. STEIGRAD (Sydney) said that inferences of a veiled nature had been made at that morning's session about the surgical members of the Association. Dr. Steigrad congratulated the Association on the fact that surgeons were present, so that, occasionally, they could come down from the rarefied atmosphere of the sublime to the mundane and ridiculous level of the practical. In the present brave new world, washing machines could be bought on hire-purchase, in Sydney, without even a deposit. And so washing machines and automatic mangles were common, and the injury described by Dr. Dey was relatively common and becoming more so. Dr. Steigrad therefore thought it wise that the subject had been presented. In treating the injury, Dr. Dey urged the employment of normal surgical principles. The best really biological dressing for a burn was skin, and if the burn or wound had destroyed whole skin, then skin should be applied. If the epidermis and dermis were destroyed, and when it was realized that total skin destruction had occurred, there was no doubt that a split thickness graft was the correct treatment, and that early in the course of treatment. He thanked Dr. Dey for the intelligence and common sense and brevity of his presentation, and, particularly, for bringing the subject before them.

F. D. STEPHENS (Melbourne) asked if the friction burn was limited to the part where the wringer finally came to rest.

Dr. Dey replied that it was a local injury. There was no damage to the skin apart from the place where the arm blocked and the roller went round. The rest was only a painful crush. There was some œdema, but no serious damage, and it all passed off in a few days without the slightest trouble.

C. J. H. GIBSON (Sydney), commenting on Dr. Dey's last remark, said that there might be enough crushing to cause soft tissue injury with subsequent stiffening, particularly in the hand. Even if one got good skin cover with early healing, and no fractures, there might still be a lot of disability from fibrosis in the subcutaneous tissues and round the tendon sheaths. That called for careful and persistent physiotherapy.

Dr. Dey, in reply, said that disability from fibrosis tended to occur in adults rather than in children, and particularly in elderly people. There was, of course, a range in the reaction of the hand to trauma in different people. In some, disability was much worse than in others.

E. STUCKEY (Sydney) said that the injury was very common in America. It seemed that with more washing machines, more cases of the injury would occur. It should not be very difficult to arrange a washing machine so that there was a trip mechanism to release the wringer automatically when anything more than a certain thickness came between the rollers. The Australian Pædiatric Association could perhaps initiate some approach in this matter so that washing machine manufacturers would have to instal such a mechanism.

NORMA KELSO (Melbourne) said that it would be rather difficult, for housewives had to wash blankets, chair covers and that sort of thing, and a considerable thickness had to pass through the wringer.

Dr. Dey remarked that there was a release lever which when banged allowed the rollers to come apart.

D. GALBRAITH (Melbourne) asked what was the immediate first aid for the injury.

Dr. Dey replied that the first aid treatment was to cleanse the part and cover it with some sterile dressing, or a piece of freshly laundered linen.

HOWARD WILLIAMS (Melbourne) asked how common the injury was.

Dr. Dey replied that it was more an injury of the middle income groups, and so of private rather than public hospital practice. He had seen about a dozen examples in about two years.

T. Y. NELSON (Sydney) said that it was important to realize how extensively a child might be injured by a wringer. He had seen a child in whom not only the whole arm was drawn into the machine, but also the clothes around his neck, so that by the time the mother arrived to release him, he was asphyxiated and not breathing. His mother was a trained nurse and applied artificial respiration. He recovered, but his injury to the arm destroyed the whole of the flexor muscle group as well as the whole of the forearm.

R. SOUTHBY (Melbourne) asked whether there was any nerve injury in such cases.

Dr. Dey replied that that was not so as a rule. He asked Dr. Nelson if the loss of the flexor muscle group was immediate or rather delayed as would occur in a Volkmann's ischæmic paralysis, a long-standing fibrotic effect.

Dr. Nelson said that it was an early effect.

Diabetes Insipidus with a Normal Draught Reflex.

CLAIR ISBISTER (Sydney) read a paper entitled "Diabetes Insipidus with a Normal Draught Reflex" (see page 234).

S. WILLIAMS (Melbourne) asked whether Dr. Isbister had observed any effect of pitressin on the patient's draught reflex. Dr. Isbister said that the patient had kept accurate records of the occurrence of the draught reflex; her let-down came normally within seconds of stimulation of the nipple, and they had found that the injections of pitressin tannate did not elicit a draught. There was also no alteration in the time taken for milk to come in.

FELIX ARDEN (Brisbane) asked whether Dr. Isbister thought that there was any emotional component in this reflex, in the fact that the mother had her baby and not some inanimate electrical suction apparatus stimulating her nipple.

Dr. Isbister replied that there was a big emotional component. A lot of experimental work showed that if the posterior hypothalamus was stimulated, the draught reflex was inhibited. Sympathetic stimulation produced inhibition of the draught reflex, as did injection of adrenaline experimentally. Dr. Isbister had no doubt whatever that taking away the baby from the mother had a very drastic effect on the reflex. The thing that was so interesting in her patient was that the subjective sensation of the draught disappeared as it did in women with failing lactation, and was only gradually restored, even though her supply returned more quickly.

KATE CAMPBELL (Melbourne) said that Dr. Isbister had put the subject of lactation on a scientific basis. It was no longer a subject considered fit for only nurses and midwives.

Splenoptosis.

S. P. BELLMAINE (Sydney) read a paper in which he described two cases of splenoptosis in infancy (see page 235).

JOHN COLEBATCH (Melbourne) remarked on the clarity and the clinical honesty that characterized Dr. Bellmaine's presentation. Dr. Colebatch suggested that a liver felt one to two fingers' breadth below the costal margin in an infant was either enlarged or ptosed. With the liver one could be fairly sure of ptosis by accurate percussion. If anyone was fortunate enough to come across another case of splenoptosis, barium swallow X-ray examination might be included in the investigation in an effort to find evidence of œsophageal varices resulting from portal hypertension. That might be of more use than an actual measurement of portal pressures at operation. Dr. H. G. Hiller in Melbourne had recently been of considerable help with splenic venograms in portal hypertension, and this investigation would also be informative in splenoptosis. Finally, in the diagnosis of Gaucher's

disease, marrow puncture was often more helpful than an X-ray examination of the long bones.

KATE CAMPBELL (Melbourne) remarked that one interesting point was that the function of the spleen did not appear to be disturbed in the first child, even though the spleen was so enlarged and congested. The other thing of interest was that in young children it was difficult to know what was the normal size and position of both liver and spleen. She had encountered the difficulty some time before when she tried to find out the size and position of the liver in normal children. She asked a professor of anatomy what it should be; he pointed out that it depended very largely on the degree of the expansion of the chest. If the chest was well expanded, the liver and spleen had a good space under the diaphragm. If the chest was ill-expanded, both liver and spleen could be low and appear to be enlarged. Dr. Campbell thought that the possibility of splenoptosis further emphasized the fact that a spleen might be low and not large.

A Syndrome of Metaphyseal Fragility with Associated Hæmorrhages in the Meninges, Retina and Skin.

FREDA PLARRE (Melbourne) presented a study of ten cases of metaphyseal fragility seen at the Royal Children's Hospital, Melbourne, during the previous four years. These children had characteristic bone swellings during infancy, often associated with other lesions, due to hæmorrhages in the meninges, retinæ and skin.

Briefly reviewing the literature, Dr. Plarre said that in 1946 Caffey reported six infants, with multiple spontaneous fractures of the long bones, all of whom had subdural hæmorrhages. In 1953 Silverman had reported three more cases which exhibited the same type of multiple bone lesions, but without subdural hæmorrhages. He attributed the bone changes to unrecognized trauma in infancy.

Astley had reported a further series of six cases with similar bone lesions, but again there was no evidence of subdural hæmorrhage in any of these. He had suggested the name of metaphyseal fragility for the condition.

The series of ten at the Royal Children's Hospital, Melbourne, included five cases similar to those of Caffey with metaphyseal changes and subdural hæmorrhages, and five cases exactly similar to Astley's series in which no subdural hæmorrhages were evident.

Discussing the clinical features in more detail, Dr. Plarre said the age incidence was well defined; the onset of symptoms in the majority of cases was within the first twelve months of life, whether the patient presented with cerebral symptoms or bone swellings.

The bone-changes affected the metaphyses of the larger joints, especially the shoulders, elbows, knees and ankles. Sometimes the ribs and spine showed changes. Appearances varied from small cracks at the corners of the metaphyses to complete separation of a plate of the metaphysis with its attached epiphysis. There was often an unusual degree of hæmorrhage in the neighbouring periosteum and soft tissue, which contributed largely to the distortion and swelling of the bone ends. Changes were usually multiple, but not as generalized as in scurvy. Fresh episodes of swelling might recur at the same or different sites over a period of months or a year or two, but most of the lesions were healed by the end of the second year. Sometimes there was residual deformity, the most notable clinically being asymmetrical *genu valgum*.

Meningeal hæmorrhage usually occurred during the first twelve months of life. One patient had chronic meningeal hæmorrhage commencing when two and a half years old, and when he died at four years, post-mortem examination revealed hydrocephalus and a gross degree of pachymeningitis. Two other babies in this series died with subdural hæmorrhages.

Retinal changes were seen in four cases as flame-shaped hæmorrhages with normal optic disks. Of the four babies, two had died with subdural hæmorrhages, while the hæmorrhages in the other two cleared up, but both these children later developed squint. Another child who had extensive bone changes during infancy, but no subdural hæmorrhage, later developed squint at the age of two and a half years. She was then found to have a detached retina which possibly resulted from an earlier unrecognized retinal hæmorrhage. Astley had also reported the presence of squint with detached retina in one of his cases.

Skin ecchymoses had been prominent in some of the cases. Sometimes the episode of bone swelling or subdural hæmorrhage had been ushered in, a day or so earlier, with bruises on the face or limbs; one had two spontaneous black eyes, and occasionally nose bleeding or hæmaturia occurred. With the exception of one case, this tendency to bruise cleared up with the other symptoms after the second year.

The first case illustrated was that of a baby girl, J.B., aged four months, who presented a few hours before admission to hospital with convulsions and a bulging fontanelle. She had xanthochromic cerebro-spinal fluid under raised tension, and the fundi showed striking flame-shaped hæmorrhages with normal disks. Because scurvy was suspected, her long bones were examined by X rays, and they showed a shaft fracture of the tibia with a large amount of callus, as well as small "corner" fractures of several metaphyses. At first, these changes were thought to be syphilitic, but both the baby's and mother's response to Wassermann tests was negative. The pictorial similarity of the bone changes to Caffey's illustrations in his text-book had then been recognized. The child improved after subdural tappings, but when last seen, at the age of three years, was mentally retarded and spastic. She had bilateral internal squint. Her mother stated that the child had bruised easily between the ages of six months and two years, but had since improved. Slides were shown to illustrate the slight residual deformities of the elbow and tibia which caused little if any disability. Spasticity, mental retardation and squint were her major disabilities.

Special investigations carried out on this series of patients had yielded no positive information. Wassermann and Kahn tests gave negative results. The results of full blood examinations including platelet counts and bleeding and coagulation times were normal. One patient with severe bruising and hæmaturia had been extensively tested at the Baker Institute, but no abnormality was detected—capillary fragility was normal, and hæmophilia was excluded. Scurvy was excluded on X-ray appearances, and one patient had urinary ascorbic acid estimations, the results of which were normal.

Dr. Plarre then briefly described the case histories of four children, all of whom belonged to the same family. The eldest girl had an unusual swelling on one elbow when aged nine months. This was diagnosed, after some hesitation, as atypical osteomyelitis, as it took place before any other cases of this type had been recognized.

The second girl had recurrent episodes of bone swelling at different sites between the ages of two months and six months—again diagnosed as "low grade" multiple osteomyelitis; then during her third year she presented with valgus deformity of the knees and squint due to the presence of a detached retina. The third girl had swelling of one knee at nine months, and X-ray examination of her bones at three years of age showed healed deformities of one tibia and one radius. The fourth child, a baby boy, had been admitted to hospital when seven weeks old, previously a bonny thriving baby, with acute collapse and death within forty-eight hours from subdural hæmorrhage. He had a bruise on one shoulder when admitted, and in the fundi were flame-shaped retinal hæmorrhages with normal disks. X-ray appearances of his long bones were normal, but had he survived the hæmorrhage, he would probably have developed bone changes similar to those of his three sisters. Post-mortem examination confirmed the presence of diffuse bilateral subdural hæmorrhages.

Dr. Plarre went on to say that when Caffey reported his cases, consideration was given to the possibility of trauma producing the bone lesions, although no history of trauma was elicited. Silverman in his series ascribed the bone lesions to trauma which was either unrecognized or not admitted by the parents. Astley drew attention to the similarity of his own group with metaphyseal defects to those of Caffey's series with intracranial hæmorrhages, and suggested "perhaps the intracranial hæmorrhage is similar to that occurring around the metaphyseal defects".

In the present series it was considered that trauma could not be a major factor in the production of these lesions. A minor role could not be denied in some stages, particularly in the older children whose gait was clumsy as a result of previous lesions in the lower limbs. The presence of hæmorrhages in other sites, namely, the skin, meninges and retinæ, suggested a hæmorrhagic diathesis in these children, and the site and nature of the bone lesions would make it likely that hæmorrhages in or near the metaphyses played some part in the production of these bone lesions too. The familial pattern in the four children previously quoted was considered to be of significance in support of the viewpoint that all these lesions had a similar hæmorrhagic basis and could be regarded as manifestations of a specific syndrome.

Acknowledgement was made by Dr. Plarre to members of the staff of the Royal Children's Hospital for clinical data of the cases studied, in particular to Dr. R. N. O'Reilly, who followed closely several of the acutely ill patients; and to Dr. Arch. Miller, of Hobart, and Dr. Gwen Hewitt for patients referred.

PROFESSOR L. DODS (Sydney) said that all would agree that the presentation by Dr. Plarre provided an original and

valuable contribution to pædiatric knowledge and that this was a new clinical syndrome. During the meeting they had learned that Melbourne had more cases of poisoning amongst children, more children with sunken chests, and many more undescended testes than Sydney; but he did not feel that one could dare to assume that the syndrome described by Dr. Plarre was also much more common in Melbourne than in Sydney, and they had to admit that in Sydney they had probably failed to recognize it.

T. Y. NELSON (Sydney) did not think they had seen anything comparable to this. Dr. Plarre's explanation of the hæmorrhagic basis seemed very likely. It seemed to Dr. Nelson that there were two different types of X-ray change in the bones—the proliferative changes might well be the result of hæmorrhage, but he took it that there was an undue tendency to fracture which gave the name fragility. And that struck him as similar to pseudarthrosis of the tibia that usually followed on a tibial kyphosis. It was possible that there might be some similar pathological basis.

JOHN COLEBATCH (Melbourne) thought that he had seen one of the patients some years previously. He thought that all such cases should be reinvestigated in the light of present-day hæmatological knowledge, for it should be possible to decide the nature of the hæmorrhagic lesion if they could see the children when the hæmorrhages were present.

Dr. Plarre, in reply, said that she was particularly indebted to Dr. O'Reilly, who had followed a number of the more acutely ill patients for her while they were in hospital, and secured as good an examination as he could. In one patient with subdural hæmorrhage who died very soon after admission he found retinal hæmorrhages and just one bruise on one shoulder that was significant. Those features had been missed by the previous examiner. In other cases no record was made of retinal hæmorrhages, and more attention to those patches might reveal more cases.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held in the Anatomy Theatre, New Medical School, Frome Road, Adelaide, on September 22, 1955.

Somatic Afferent Systems.

MR. D. I. B. KERR, in a paper prepared in collaboration with W. A. STOTLER, of Portland, Oregon, reported that on the basis of degeneration studies and electrophysiological characterization, four somatic afferent paths were recognized in the cat. They could be summarized in the following way: (i) shortest latency, medial lemniscus, contralateral, terminating in the *nucleus ventralis postero-lateralis*; (ii) short latency, spino-bulbo-thalamic, bilateral, terminating in the *nucleus ventralis posterior*; (iii) medium latency, central tegmental fasciculus, bilateral, terminating in phylogenetically older medial thalamic nuclei; (iv) longer latency, central grey, bilateral, traced to the periventricular area. In addition longest latency "reticular" responses were found scattered in the ventral mid-brain tegmentum and subthalamus. Analogous paths from the trigeminal system were identified.

Incompatibility Systems in Higher Plants.

MR. D. L. HAYMAN presented a paper on incompatibility systems in higher plants. He said that a system of outbreeding maintained a higher level of heterozygosity in a population than a system of inbreeding under specified conditions. That conferred several advantages to populations. Incompatibility was a genetically controlled means of ensuring outbreeding. It imposed a physiological barrier to gametes which came together in the wrong genetical and physiological combinations. The effect of that barrier on incompatible pollen grains was to reduce the germination percentage or the growth rate, and even to cause a breakdown of the fertilization process. Several different genetical systems of controlling incompatibility had been found. In general plants in the same taxonomic family had the same system. The evidence in favour of the physiological basis of incompatibility being analogous to the antibody-antigen reaction in animals was presented.

Special Correspondence.

NORTH AMERICAN LETTER.

FROM OUR SPECIAL CORRESPONDENT.

Graduate Training in Neurology.

OF the several National Institutes of Health set up in Washington, D.C., few have shown the interest in graduate training now displayed by the National Institute of Neurological Diseases and Blindness. This Institute has made a large grant to the Graduate School of Medicine of the University of Pennsylvania in Philadelphia, which for the next two years will conduct special courses in graduate medical training in neurology. The courses are designed for those who will engage upon full-time academic work or research in these specialties. Men nearing the time of certification as specialist in their training may be nominated for these fellowships by their home medical school on the understanding that they will return to their own departments eventually for teaching and research purposes.

The objectives of these fellowships are threefold: (*a*) to improve the teaching ability of capable neurologists, (*b*) to provide a good scientific background for medical research, and (*c*) to provide advanced training in the candidate's home university in neurology and neurological sciences generally upon his return.

This emphasis on some training in pedagogy is long overdue in many medical quarters. In this particular instance the post-graduate students will take turns in lecturing and will have their lectures recorded on tape, in order that each lecture may be played back and reviewed for its weak points and its strong points. Special emphasis is to be given to medical writing and the use of all the services of a modern medical library. Basic sciences in particular will be studied, with emphasis naturally on the neurological phases of physiology, pharmacology, biochemistry, anatomy, pathology and microbiology.

To equip these neurologists with some of the basic requirements for good research programmes, courses are being provided in mathematics, statistics, the design of experiments, recent advances in physics, chemistry and electronics, newer methods of investigation, and critical evaluation of the medical literature. Many teachers, researchers and clinicians will take part in the instruction here.

Clinical work will be no mere repetition of what the partly trained neurologist has already done, but will be branching out into more responsible fields; advanced seminars, student teaching and investigative work will all be combined. The successful candidates will qualify for the degree of Doctor of Science (Med.). The same type of emphasis is being used in a parallel course in ophthalmology in the same graduate school.

Federal Mental Health Grants in Canada.

Beginning in 1948, the Federal Government of Canada set up a system of Mental Health Grants for specific projects approved for each province. The money could be spent on mental hospitals, training schools for nurses and technicians, psychiatric services within general hospitals, mental health clinics for adults or for children, travelling clinics, the training of social workers, bursaries for post-graduate research, the needs of existing mental hospital staffs and so on. In the first year approximately $4,000,000 was available for this, and the sum has now risen to well over $6,000,000.

One of the greatest effects of this programme has been to stimulate the growth of mental health clinics. In 1948 there were only 14 full-time clinics in the country of a public nature. Most of these were in the school systems of large cities, and there were in addition five part-time clinics. However, by 1954 there had developed in the country 14 psychiatric clinics within general hospitals, 66 out-patient units whether at general hospitals or mental hospitals, and 101 mental health clinics, such as travelling clinics and child guidance clinics; and as at last year there were 286 full-time and 184 part-time employees in the 55 mental health clinics and a large number of people away in training whose return was anticipated to increase further the services to the public.

In the six-year period from 1948 to 1954 a total of 11,929 beds were added to existing installations across the country. This number is still, of course, far short of what is required for mentally deficient children and for senile patients.

The problem of recruiting trained personnel remains a very serious one in Canada. The Federal Health Grants have enabled hospitals to train 225 psychiatrists, 139 psychologists, 138 psychiatric nurses, a similar number of psychiatric social workers, 20 electroencephalographic technicians, and 15 occupational therapists. Further expenditures of this nature will be required if Canada is to maintain competent personnel in its public institutions against the recurring raids of American institutions across the border. The problem of salary levels is most acute, and with much larger rewards in private practice and in teaching posts the publicly operated mental hospitals have obviously to be given much more tax support than they are now getting if they are to maintain a staff. There is nothing more demoralizing than the constant ebb and flow of trained personnel in these institutions. There is a widespread desire, especially in the medical profession, to see the salaries of physicians in the public service levelled up instead of levelled down. Competition with other governmental agencies, such as the Armed Forces and Defence Research Board, has brought home clearly to administrators in recent years the need to lead the field in rewards offered, not to trail in it.

Rehabilitation, preventive work and research would seem to be the great fields in which Federal aid can best be applied in the future. Volunteer programmes sponsored largely by the Canadian Mental Health Association, a lay association with no official connexions whatever, are beginning to have a great effect. Service clubs, junior chambers of commerce and so on are finding the work very rewarding, not only because it helps mental patients ready for rehabilitation in the community, but because of what it does for the members of the volunteer groups themselves. In research projects the Federal grants this year will probably amount to well over half a million dollars.

Correspondence.

TOTAL ADRENALECTOMY AND OOPHORECTOMY FOR CARCINOMA OF THE BREAST.

SIR: I welcomed Dr. Basil Stoll's criticism of my article on total adrenalectomy. Dr. Stoll has evidently had extensive experience in the treatment of carcinoma of the breast with metastases, and one must respect his opinions.

I may have given the impression that adrenalectomy and oophorectomy was my first line of attack, but I can assure Dr. Stoll that up to the present this has not been the case. A careful selection of cases has been made, but the improvement in the ones who have responded has perhaps led me to offer this palliative treatment at an earlier date than previously. I am well aware of the benefits derived from palliative irradiation of bone metastases, but in my experience the relief from pain with irradiation is not equal to that obtained from adrenalectomy for carcinomas which are hormonally controlled. Many of my patients who have had irradiation and who have been bedridden with pain have been able to walk and move around completely free from pain after adrenalectomy. If relief from pain is not obtained by adrenalectomy, one assumes that the carcinoma is not hormonally dependent, and irradiation can be used after the adrenalectomy with very good effect.

Dr. Stoll suggests that prolonged trials on irradiation, testosterone, castration and cortisone will give the surgeon a lead as to whether adrenalectomy or hypophysectomy will be of benefit. Charles Huggins and Sir Stanford Cade state that there is no known method of determining which cases will respond, but intensive research is proceeding at present, and they think that within two years we will have reliable hormonal tests which will give us this information.

Dr. Stoll's trial treatment of patients with established metastases seems to extend over three to five years. It is asking a great deal of adrenalectomy and also of hypophysectomy to effect a cure or even alleviation in patients who have widespread dissemination of the disease for that length of time. My patients with established metastases do not live long enough to give all these methods a prolonged trial.

A twelve months' trial on cortisone in my opinion is time lost; this amounts to a chemical adrenalectomy and is not as effective as surgical treatment; it can be classed in the same category as irradiation castration versus oophorectomy.

I have not had the happy experience with testosterone which Dr. Stoll seems to have obtained in a very extensive series of cases. I still maintain that it is a waste of time giving testosterone and only makes the patient mentally disturbed and unhappy; the physical disturbances I ignore. Surgical oophorectomy on its own has not given me satisfactory results.

I still maintain that in cases which respond to adrenalectomy the improvement in metastases and general well-being far outweighs any other accepted methods of treatment. Only this week I reviewed a patient who came to me from Queensland in July, 1955, with extensive metastases in the thoracic and lumbar spine, a red blood cell count of 2,000,000 per cubic millimetre and a hæmoglobin of 5·3 grammes *per centum*. This patient had an oophorectomy and adrenalectomy in August. She presented herself for a re-ray this month with all her spinal metastases completely recalcified and not visible on the films. She looks well and declares she has not felt so well for three years. Her blood count is normal, and she is maintained on 37·5 milligrammes of cortisone daily. Whilst I continue to get some patients with these excellent results I feel that one should offer the treatment to suitable patients, not at the end of two, three or four years' treatment on other methods of alleviating metastases, but possibly at an earlier stage than we have hitherto considered.

Of hypophysectomy I have no personal experience, but I am anxious to give this method a trial in collaboration with a neurosurgeon. Dr. George Pack, in a lecture under the ægis of the Post-Graduate Committee in Medicine at the Stawell Hall in Sydney this week, stated that hypophysectomy is an extremely difficult operation, and it is very hard to be sure that the whole of the pituitary gland had been removed. My impression of his views was that hypophysectomy should be reserved for cases in which adrenalectomy had shown no improvement.

Yours, etc.,

141 Macquarie Street, Sydney,
January 27, 1956.

K. CUNINGHAM.

OBSERVATIONS UPON 250 CASES OF BLEEDING PEPTIC ULCER.

SIR: In his letter dated January 10, appearing in your issue of January 21, Dr. K. W. Manning again describes as "platitudinous and vague" the factors which I suggest should be weighed in the diagnostic balance in an endeavour to select those patients with bleeding peptic ulcer who might benefit by surgery. Actually, he describes these factors as "formulæ" and demands that the indications for use of surgery be stated "in precise and exact terms". He wishes to know: "At precisely what point does one decide that a given case has 'failed to stop bleeding'? At what stage in terms of hours or minutes is it decided that the 'initial hæmorrhage continues despite treatment'?"

It would appear that he would give no place to clinical judgement reached after carefully weighing all the factors known or reasonably suspected. He cannot believe that "each case is to be regarded as a special problem deserving of the most careful attention", as is so aptly described by Sir Gordon Gordon-Taylor in his First Lettsomian Lecture in 1945, a contribution well worth studying. I suggest, sir, that nothing in medicine can ever be blindly followed by any "formula", a method more applicable to the field of mechanics than the practice of medicine.

That Dr. Manning finds it difficult to be sure when the initial hæmorrhage has ceased or when bleeding recommences is, of course, not surprising, for the difficulty is universal because of the very facts he mentions. However, this difficulty can be no excuse for giving up the challenge of selection.

It is not necessarily true that when severe bleeding occurs at "a certain rate the patient is doomed" and "no opportunity exists for surgical treatment", for in several such cases, with vigorous resuscitation, expert anæsthesia and urgent surgery, a life has been saved which may well have been considered "doomed" by the more pessimistic physician.

I can only reiterate—more forcibly, if possible—that I do consider it "the height of foolishness", "courting disaster"

and "putting the clock back twenty years" to advocate restricting transfusion to the extent of withholding blood "unless there was recurrence of significant bleeding in a patient whose hæmoglobin value was already in the region of four or five grammes *per centum*". It was in 1935 that Marriott and Kekwick instituted drip transfusion, the most important single factor in saving life in gastro-duodenal hæmorrhage. Such withholding of transfusion as advocated by Dr. Manning may well lead to the development of a degree of anoxæmia, which, in turn, is liable to cause restlessness and lack of cooperation at all ages, and coma and irreversible shock in the elderly. Severe anæmia itself embarrasses the heart by increasing the cardiac output. Such a degree of anæmia is no help to the patient if he is asked to withstand any further "significant bleeding".

In my own experience I have been fortunate in working with physicians who believe in the value of early consultation between physician and surgeon and have had the opportunity of seeing a reasonable number of these cases; the exact number of these cases seen in consultation I cannot recall, but have in the last seven years operated upon 32 of these patients, with only one death.

I would point out that Dr. Manning's impression that "free transfusion tended to cause recurrence of bleeding" is not the result of experience of "hundreds of cases", for in his review of 250 cases there were only 59 or, as he would have it, 53 cases, with recurrent bleeding, and it is only his experience with these which could permit of this impression.

Lastly, sir, I would point out that while the mortality rates for surgery in these patients is greater than that for elective surgery, it is not "considerable", and venture to suggest that with careful cooperation between physician and surgeon the indications for operation may well be widened and lead to a less significant mortality.

Yours, etc.,

185 Macquarie Street, Sydney,
January 26, 1956.

NOEL C. NEWTON.

Obituary.

JOSEPH GOLDMAN.

DR. T. E. WILSON has sent the following appreciation of the late Dr. Joseph Goldman.

Joseph Goldman was born at Bombala, New South Wales, on April 14, 1901. His boyhood was spent with his seven brothers and sisters in the country, where he loved the outdoor life, especially the shooting, swimming and fishing. His early education was at Saint Joseph's College, Sydney, which he represented in the Great Public Schools cricket matches. In addition to being a keen cricketer and a good left-hand googly bowler he was an able tennis player. After graduating from the University of Sydney in 1924 he held appointments as resident medical officer at Sydney Hospital for two years. He then proceeded to general practice, first at Lowood, Queensland, and later at Fairfield, New South Wales. In 1933 he moved to Maroubra, where he built up a very large but personal practice. From 1942 to 1944 he served in the Australian Army Medical Corps and then returned to Maroubra, where he was joined by his brother, Dr. Maurice Goldman, and by Dr. Lyn Joseph. On December 30, 1955, whilst he was swimming with his daughter, Dr. Sonia Goldman, a freak wave washed them out to sea. His daughter was rescued, but Dr. Joseph Goldman was drowned before help could reach him.

Joseph Goldman had a happy personality, and with his inborn kindliness possessed a great number of friends. It is difficult to realize that Joe is no longer with us and that we have been deprived of his friendship in the years to come. He was an outstanding doctor and could well be cited as an example of the ideal family practitioner. He was modest and courteous by nature, efficient in his work, with good clinical judgement, and not concerned with self-advancement. On the other hand, he was very interested in his patients and their welfare. This was shown by the trust and faith they had in him, by their affection for him, and by the large number who attended his funeral service. They, in addition to his family and friends, will greatly miss him. He is survived by his wife, a son (Dr. Louis Goldman) and two daughters (Sonia and Janice).

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

ABORIGINAL OBSTETRICS.[1]

[From "An Historical Journal of the Transactions at Port Jackson and Norfolk Island", by John Hunter, Esq., Port Captain in His Majesty's Navy, London, 1793.]

August, 1791.

BANNELONG'S wife was now very near her time, which gave our colonists an opportunity of seeing the preparations the women of New South Wales make on these occasions: she had two nets hanging from her neck, one of which, being new, Governor Phillip was desirous of obtaining, and it was given him, after she had taken a large piece of the bark of the tea-tree out of it, nicely folded up, and which was intended to lay her infant upon: this seems to be the only preparation which is made by lying-in women in that country. The bark of the tea-tree is thick in proportion to the tree and is composed of a great number of layers of very thin bark, in appearance not unlike the bark of the birch tree: but it is so very soft that nothing this country affords can be better calculated for the purpose for which it was intended: Bannelong however desired to have a blanket for the child, which was given him, and the next day, a net made in the English manner, which appeared more acceptable to his wife than the one she had parted with. He told Governor Phillip that his wife intended doing him the honour of being brought to bed in his house: but the Governor at length persuaded him that she would be better accommodated at the hospital. The women do not appear to suffer any great inconvenience, while in this state, and they all seem pleased with having boys.

Australian Medical Board Proceedings.

QUEENSLAND.

THE following have been granted limited registration as medical practitioners, pursuant to Section 20 (3) of *The Medical Acts*, 1939 to 1955, of Queensland: Fraser, Hugh Barron, M.B., B.S., 1955 (Univ. Adelaide); Brookes, Ronald Alfred, M.B., B.S., 1955 (Univ. Sydney); Reid, Leslie Robert, M.B., B.S., 1956 (Univ. Sydney); Tait, Maxwell Stuart, M.B., B.S., 1955 (Univ. Melbourne); Allen, Eric Abbott, M.B., B.S., 1956 (Univ. Sydney).

The following has been registered, pursuant to the provisions of Section 19 (1) (*b*) of *The Medical Acts*, 1939 to 1955, of Queensland, as a duly qualified medical practitioner: Sunderland, Ian McKenzie, M.B., Ch.B., 1954 (Univ. Leeds).

The following additional qualifications have been registered: Gallagher, Maurice John, F.R.C.S. (England), 1954; Evans, Cyril Percival Victorious, D.T.M. (Sydney), 1946, M.R.C.P. (London), 1953; Earnshaw, Beatrice Averil, D.A. (London), 1953, F.F.A., R.C.S. (England), 1955; Power, John Joseph, M.C.R.A., 1955; Campbell, Charles Haxton, M.R.A.C.P., 1954; Douglas, Gavin James, F.R.A.C.S., 1956.

Post-Graduate Work.

SEMINARS AT ROYAL PRINCE ALFRED HOSPITAL.

SEMINARS will be held on the following dates from 1.15 to 2.15 p.m. in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital, Sydney:

February 17, cardio-vascular section, "Aortic Stenosis", Dr. John Halliday. February 24, endocrinology and metabolism

[1] From the original in the Mitchell Library, Sydney.

section, "Current Concepts in Endocrinology", Dr. Peter Hall. March 2, thoracic section, "Physiotherapy in Respiratory Disease", Dr. M. R. Joseph and Miss J. Gardiner. March 9, gastro-enterology section, "Study of 500 Cases of Hæmatemesis", Dr. R. S. Packard. March 16, neurology section, "The Basilar Artery and its Syndromes", Dr. J. L. Allsop and Dr. Brian Turner (by invitation). March 23, hæmatology section, "The Anæmias of Pregnancy", Dr. J. M. Farrar and Dr. Mary Heseltine. April 6, cardio-vascular section, "Coarctation of the Aorta", Dr. B. C. Sinclair-Smith. April 13, endocrinology and metabolism section, "Porphyria", Dr. T. M. Greenaway. April 20, thoracic section, "The Treatment of Emphysema", Dr. Peter Harvey and Dr. Alexander Grant. April 27, gastro-enterology section, "Ulcerative Colitis" (Part I), Dr. A. W. Morrow and Dr. S. J. M. Goulston. May 4, neurology section, "Tuberculous Meningitis: A Modern Assessment of Treatment and Prognosis", Dr. H. M. Rennie, Dr. Kerr Grant (by invitation) and Dr. Peter Harvey. May 11, hæmatology section, "Fibrinolysis", Dr. Barry Firkin (Dr. J. M. Farrar will open the discussion). May 18, pædiatrics section, "Hirschsprung's Disease in Infancy", Dr. S. P. Belimaine and Dr. John Loewenthal (to be followed by a clinical meeting at 4 p.m. at the Royal Alexandra Hospital for Children, Camperdown). May 25, cardio-vascular section, "Pulmonary Hypertension", Dr. Keith Cotton. June 1, renal section, "Treatment of Nephritis", Dr. S. R. Reader and Dr. D. J. Deller. June 8, endocrinology and metabolism section, "Serum Proteins in Clinical Medicine", Dr. Barry Firkin. June 15, thoracic section, "Observation Error in Chest X-Ray Interpretation", Dr. John Read. June 22, gastro-enterology section, "Ulcerative Colitis" (Part II), Dr. A. W. Morrow and Dr. S. J. M. Goulston. June 29, neurology section, "Experiences Abroad in the Neurosurgical Field", Dr. G. K. Vanderfield. July 6, hæmatology section, "The Hæmoglobins", Dr. E. F. Thomson and Dr. C. R. B. Blackburn.

The following will be the programme on each Friday afternoon: seminar, 1.15 to 2.15 p.m.; clinico-pathology, 2.15 to 3.15 p.m.; tea, 3.15 to 3.30 p.m.; unit rounds, 3.30 to 5 p.m.; grand rounds, 5 p.m. to 6 p.m. Apart from unit rounds, these sessions will be conducted in the Scot Skirving Lecture Theatre.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned apointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 5, of January 26, 1956.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Confirmation in Rank.—Surgeon Lieutenant (for Short Service) (on probation) William Aloysius O'Brien is confirmed in the rank of Surgeon Lieutenant (for Short Service), with seniority in rank of 12th October, 1954.

Termination of Appointment.—The appointment of Michael Francis Bennett as Surgeon Lieutenant (for Short Service) is terminated, dated 1st December, 1955.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Appointment.—John Francis Walsh is appointed Surgeon Lieutenant, dated 27th July, 1955.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps.

2/40180 Captain E. H. Holland is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Eastern Command), 9th December, 1955.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—1/39147 Major C. C. Wark, M.B.E., is appointed to command 2nd Casualty Clearing Station, and to be Temporary Lieutenant-Colonel, 1st October, 1955.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JANUARY 21, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	8(6)	3(2)	5(3)	1	1	..	..	..	18
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1(1)	1	3	..	..	..	..	..	5
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4(3)	9(8)	3(3)	..	4(4)	..	..	1	21
Diphtheria	..	5(5)	..	..	3(2)	..	..	..	8
Dysentery (Bacillary)	..	..	5(5)	..	4(3)	..	..	..	9
Encephalitis	2(1)	..	..	1	..	..	..	..	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	56(34)	96(44)	..	3	7(3)	..	1	1	164
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1(1)	4(3)	..	..	1	..	..	..	6
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	6(3)	6(3)	3(3)	3(3)	32(23)	..	..	1	51
Puerperal Fever	..	..	1	..	..	..	1	..	2
Rubella	..	87(58)	..	6(2)	1	..	..	..	94
Salmonella Infection	..	..	..	1(1)	..	..	..	..	1
Scarlet Fever	6(4)	7(2)	6(1)	13(3)	2(2)	..	..	..	34
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	2(2)	..	..	..	2
Trachoma	..	..	..	..	2	..	..	..	2
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	37(15)	20(14)	..	9(6)	9(9)	5(2)	..	1	81
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	1(1)	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

1/39015 Lieutenant-Colonel E. P. Row, E.D., relinquishes command 2nd Casualty Clearing Station, 30th September, 1955.

1/39086 Captain W. H. Tait is appointed from the Reserve of Officers, 23rd November, 1955.

1/61768 Captain (Honorary Major) P. J. Monahan is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Northern Command), 27th September, 1955.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—To be Temporary Majors, 9th December, 1955: Captains 2/206956 G. L. McDonald and 2/206958 W. R. M. Shaw. To be Captain (provisionally), 24th November, 1955: 2/147954 Herbert John Keogh.

Southern Command.

Royal Australian Army Medical Corps (Medical).—To be Temporary Major, 1st December, 1955: 3/101016 Captain R. D. Wilson. The provisional appointment of 3/129011 Captain A. M. Marshall is terminated, 7th July, 1955. To be Captains (provisionally): 3/129011 Alan Morrison Marshall, 8th July, 1955, and 3/139406 Michael Rupert Barrett, 7th December, 1955.

Western Command.

Royal Australian Army Medical Corps (Medical).—To be Major, 2nd December, 1955: 5/15975 Captain (Temporary Major) D. C. Foster.

Tasmania Command.

Royal Australian Army Medical Corps (Medical).—6/15257 Captain J. S. Elliot is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Southern Command), 29th November, 1955.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

Northern Command.—To be Honorary Captains: Frank Kennedy Fry, 18th November, 1955, Gwenyth Jean Havig, and Peter Gordon Livingstone, 21st November, 1955.—(Ex. Min. No. 216—Approved 18th January, 1956.)

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Sarko, Nikolai, regional registration: for practice in the Premer Region, Premer, New South Wales.

Deaths.

THE following deaths have been announced:

ROXON-ROPSCHITZ.—Isador Roxon-Ropschitz, on January 23, 1956, at Brisbane.

SHIPWAY.—Graham Stuart Shipway, on January 26, 1956, at Victor Harbour, South Australia.

WILSON.—William Edgar Wilson, on January 26, 1956, at Melbourne.

STEEL.—Mark Steel, on January 27, 1956, at North Sydney, New South Wales.

Medical Appointments.

Dr. Keith McLeod Benn and Dr. James Graham Duram have been appointed senior medical officers in the Mental Hygiene Branch of the Department of Health, Victoria, pursuant to the provisions of Section 18 (2) of the *Mental Hygiene Authority Act*, 1950.

Dr. J. R. Barbour has been appointed honorary orthopædic surgeon, Royal Adelaide Hospital, South Australia.

Dr. N. P. Wilson has been appointed honorary assistant orthopædic surgeon, Royal Adelaide Hospital, South Australia.

Dr. W. J. Betts has been appointed honorary assistant orthopædic surgeon, Royal Adelaide Hospital, South Australia.

Dr. S. P. Barnett has been appointed honorary clinical assistant to the orthopædic section, Royal Adelaide Hospital, South Australia.

Dr. I. M. H. Camens has been appointed honorary assistant visiting medical officer, infectious diseases section, Northfield Wards, Royal Adelaide Hospital, South Australia.

Diary for the Month.

FEB. 13.—Victorian Branch, B.M.A.: Finance Subcommittee.
FEB. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
FEB. 16.—Victorian Branch, B.M.A.: Executive of Branch Council.
FEB. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
FEB. 22.—Victorian Branch, B.M.A.: Branch Council.
FEB. 23.—South Australian Branch, B.M.A.: Scientific Meeting.
FEB. 24.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 25.—Tasmanian Branch, B.M.A.: Annual Meeting.
FEB. 28.—New South Wales Branch, B.M.A.: Ethics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 8 King's Park, West Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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